833

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PHYSIOLOGY OF THE ANEMIAS: NORMAL AND PATHOLOGIC.*

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Anemia is a term applied to a reduction of erythrocytes and hemoglobin and likewise the clinical syndrome which may result. For a proper understanding of the physiology of the anemias it is necessary to consider the physiology of blood formation and disintegration and how the two processes are kept constant.

In infants at birth the erythrogenetic islets showing blood forming activity are found not only in the red bone marrow, but also in the liver, spleen, and lymphatic tissues. After a few months the erythrogenetic function becomes limited to the red bone marrow of all the bones where it remains localized until about the sixteenth year. After the sixteenth year the site of the formation of erythrocytes becomes further limited to the flat bones, small spongy bones, and heads of long bones.

In the adult, with excessive blood destruction and consequent need for new erythrocytes, the function in these infantile situations may be resumed to meet the need for increased output in the dire emergency, but the liver is called upon only in the most extreme need.

Histologically,[1, 2] the bone barrow is a very plastic tissue enclosed in a rigid case of bone and consists of fat cells; a blood vascular system made up of arterioles, venous sinuses and veins; and blood forming islets supported by a reticulum. The arterioles are thick walled, while the sinuses have very thin walls made up of a single layer of endothelial cells. The fat cells and erythrogenetic islets lie between these venous sinuses. The erythrocytes grow in very definite groups in the reticulum of the bone marrow, the nucleated cells and cells showing mitosis being centrally arranged in the grouping, with the cells toward the periphery becoming more and more of adult type. The adult cells thus come to lie in contact with the thin endothelial cells constituting the walls of the venous sinuses.

The passage of erythrocytes from the erythrogenetic islets to the blood stream is explained by Drinker[3] as follows. In the normal adult with steady growth by central expansion, we have the result of growth in a closed space and the cells are thereby forced into the circulation. The venous siuuses of the bone marrow contain blood at a very low pressure and it is into these yielding structures that growth steadily forces the adult erythrocytes that are being constantly produced in the erythrogenetic islets to keep pace with the constant disintegration of worn out cells in the peripheral blood stream.

Just what it is that keeps the rate of reproduction of erythrocytes at a definite pace with the destruction of erythrocytes—called "hemogenic-hemolytic balance"—is not definitely known. Leake[4] thinks that the growth of new red cells would be regulated more or less by demand, that the rate of production and entry of new red cells would be regulated by the rate of removal from the blood stream. This would imply some sort of hormonal regulation probably between the spleen and the red bone marrow. Drinker and Drinker[5] have shown that the arterioles entering into the venous sinuses in all cases appear to be supplied by vasomotor nerves, other nerve filaments being distributed through the blood forming tissue outside the vessels. These nerves appear to be afferent in character but the possible nerve control of the cellular secretion of the blood forming tissue is almost an unexplored field. Drinker[6] also states that the need for hemoglobin is the stimulus maintaining blood formation at its balanced level. Adult erythrocytes probably cannot increase their hemoglobin content and we must therefore look for more hemoglobin not in terms of augmented old cells, but in terms of new cells per unit volume of blood.

Normally, the erythrocytes in the adult male number about 5,000,000 or 5,500,000 in a training athlete, per cubic millimeter of blood and

*Read as a part of the symposium on "The Anemias" at the fifty-ninth annual session of the Medical Society of Virginia, in Danville, October 16-18, 1928.

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in the female 4,200,000 to 4,500,000. At birth the erythrocytes number about 7,000,000 per cubic millimeter of blood and the count falls until the end of the first year when it is about 3,500,000 per cubic millimeter of blood. After this time there is a gradual rise to reach the adult count at the sixteenth year, the count remaining constant until the sixty-first year, when a slight gradual but steady fall begins. Thus it is seen that there are fluctuations in the number of erythrocytes associated with age and sex and it must be remembered that there are also diurnal variations in the erythrocyte count reported by Leake. Kohl and Stebbins.[7] In observations on healthy men and women from eighteen to thirty years of age the average diurnal variation in the erythrocyte count was 350,000 for the men and 310,000 for the women. Also the average source of error of plus or minus 2 per cent in the enumeration of erythrocytes should be kept in mind. One should be somewhat indifferent to variations in erythrocyte counts when such variations do not exceed 250,000 cells pur cubic millimeter of blood. Thus, too great a devotion to numerical expressions would not appear to be warranted.

The shape of a normal erythrocyte is that of a biconcave disc. An odd shaped erythrocyte is termed a poikylocyte. Huck and Bigelow[8] and Sydenstricker[9] state that odd shaped erythrocytes may appear in the blood of individuals in whom there is no fundamental blood disease. Poikylocytosis mentioned in the text books as evidence of blood destruction, therefore, may appear in otherwise normal blood as a familial anomaly. The size of a normal erythrocyte averages 7.5 microns and this measurement is fairly constant. A variation in size is termed anisocytosis, the cells larger than normal being termed macrocytes or megalocytes, and cells smaller than normal are termed microcytes.

Erythrocytes have staining characteristics which are diagnostic. When stained by the supravital method some show a coarse skein or network of granular filaments. These are called reticulated cells and this reticulation appears to be a characteristic of very young erythrocytes. The number of reticulated cells in the circulating blood is probably the best available index of activity in blood regeneration. An increase in the number of these cells may be interpreted as indicating both an excessive demand for new cells and a competent bone marrow. The normal percentage of reticulated cells is .3 to 1 per cent of all the erythrocytes. Polychromatophilic erythrocytes are those which have taken up some of the basic stain as well as the acid stain giving the erythrocytes a faint bluish color, which is also characteristic of very young cells.

Blood platelets are formed from the megakaryocytes of the bone marrow.[10] The megakaryocyte is a giant cell found wherever red blood cell forming tissue is found, and has a single ring-shaped nucleus made up of a number of large vesicular nuclei lying with edges overlapping and apparently fused together. By ameboid movement and also by the pressure of growth these cells enter into the venous sinuses of the blood forming tissue where they break up into blood platelets. The blood platelets are the principal source of prothrombin, an indispensable factor in the coagulation of the blood. Megakaryocytes are rarely in the blood stream, but are filtered out in the lungs on account of their large size. The normal blood platelet count, enumerated by direct method, ranges from 250,000 to 350,000 per cubic millimeter of blood. Physiologic variations in the number of platelets are marked since they increase at high altitudes, are higher in winter than in summer, and vary from day to day. Thus a single count should not be relied upon. There is also a greater unavoidable source of error in counting platelets than in counting erythrocytes, but the count is accurate enough for ordinary clinical purposes, since only a very great variation in the count would have clinical significance.

The origin of hemoglobin would appear to be in considerable doubt even yet. The materials from which it is synthesized are derived in the metabolism of food and from conserved pigment and iron remaining in the liver from the breakdown of hemoglobin of previously destroyed erythrocytes. The factors necessary for the actual synthesis remain obscure but it would appear that sunlight and certain accessory food factors are significantly involved. The actual place of formation of hemoglobin from its components seems to be in the red bone marrow and it appears in the erythrocytes during some stage of their formation. Normally, the amount for each erythrocyte is fairly constant. The color index indicates the amount of hemoglobin in each erythrocyte

compared with the normal amount. The normal color index is one which is obtained by dividing the percentage of hemoglobin by the percentage of erythrocytes. When an abundant supply of building material is available, the bone marrow may build an excess of hemoglobin into the erythrocytes giving a high color index. This is seen in some hemolytic anemias where the iron containing portion of the liberated blood pigment is retained in the body for future building of hemoglobin and the non-iron containing portion is eliminated as urobilin. If the iron is lost by hemorrhage or the bone marrow is unable to utilize the materials at hand, the erythrocytes are deficient in hemoglobin and the color index is low. The lowest color index is found in chlorosis, where the materials cannot be used and in post-hemorrhagic anemia where the iron is lost. This, of course, is only one of many explanations for the color index.

Now, as to the methods by which worn out erythrocytes leave the circulation: Rous[11] states that there are two methods by which this takes place—(1) fragmentation anywhere in the blood stream with the fragments lodging in the spleen and other organs rich in reticuloendothelial cells; (2) phagocytosis which takes place chiefly in the spleen. The average span of life of an erythrocyte in the blood stream is estimated by Addis[12] to be about fourteen days; by Ashby[13] about thirty days Addis[14] also estimates that 7 per cent of the total number of erythrocytes in the body disintegrate daily, which would be 1,750,000,000,000 erythrocytes destroyed daily and a proportionate amount of iron removed from the circulation. Although this enormous number of erythrocytes are disintegrating daily they have a normal resisting power which can be measured by subjecting them to the action of various harmful agents. This is called the fragility test and the reagent generally used is a hypotonic salt solution. Normal erythocytes will not begin to hemolize until the salt solution reaches .44 or .42 per cent. By this test it is possible to determine if an excessive hemolysis is referable chiefly to increased fragility of the erythrocytes, or to an excessively toxic hemolytic agent acting upon erythrocytes of normal resisting power.

It is important to keep in mind the distinction between erythrocytes and hemoglobin and to remember that hemoglobin is organized in the erythrocytes and is the essential material for providing the cells of the body with the oxygen necessary for life. It does not bear any constant relation to the number of the erythrocytes. Hemoglobin content varies with age and sex and there is a diurnal variation worked out by Mills[15] and Gram[16]. In estimating the hemoglobin, Leake[17] found the limit of error to be about plus or minus 5 per cent with the usual clinical methods. Here also, as with the erythrocytic percentage, unwarranted devotion to numerical expressions would appear to be unwise.

The custom of recording hemoglobin in percentage terms is grossly inaccurate and leads to much confusion. The situation is further complicated by the fact that hemoglobinometers in general use employ different standards, and a specimen of blood which reads 100 per cent on the Dare instrument, for example, will read about 80 per cent on the Sahli, 81 per cent on the Newcomer, and about 87 per cent on the Tallquist, if the calibrations are in accordance with the claims of the several makers. A record therefore means little unless one knows what instrument was used and the age and sex of the patient. This confusion could be avoided if records were made in actual percentage of hemoglobin that is, grams per 100 c.c. of blood. This plan has been adopted by certain large hospitals and has been proposed by the American Society of Clinical Pathologists for consideration as a standard method. The reading on any type of instrument can be easily converted into grams if one knows what amount of hemoglobin was adopted as the standard representing 100 per cent. Lindsay, Rice and Selinger[18] have suggested 14 to 17 grams per 100 c.c. as the normal limits of hemoglobin content of the blood, these figures being used in the same manner as the normals in blood chemistry. This would correspond to 83 to 101 per cent on the Newcomer hemoglobinometer which some investigators[18, 19] recommend as the best instrument for clinical work.

Keeping in mind the normal blood picture, and differences from the academic normal which are not greater than the average variation, and thus may for all practical purposes be considered normal, we may pass to a brief consideration of the physiology of the clinical types of anemias.

Clinically, it is customary to divide anemias

into two groups termed, "secondary" and "primary", and, although this classification has its shortcomings, it has long been in general use and will be adhered to now because it is convenient and easily followed.

Secondary anemias are symptomatic of some underlying pathological condition, while primary anemias appear to develop and progress independently of any other concomitant disease. It is not always easy to make the distinction between the two groups, although each has a more or less distinctive and characteristic blood picture.

In secondary anemias the blood changes vary somewhat with the cause, but in general the blood picture is so similar for all cases of secondary anemia of the same severity that we may consider them as a group.

Diminution of hemoglobin is the constant and most characteristic feature of secondary anemias. In mild cases it may be slight, usually 60 to 70 per cent; in severe cases 40 to 50 per cent, and in extreme cases 15 per cent or even less. The color index may be reduced as low as .8 to .7 but rarely as low as .5. The leucocytes do not bear any direct relation to the anemia but neutrophilic leukocytosis is common. In mild cases stained films show no appreciable change, but in moderate to severe cases there will be seen anisocytosis, poikilocytosis, some polychromatophilia and even occasional nucleated erythrocytes. The severe forms also show basophilic degeneration and small or considerable numbers of nucleated erythrocytes as noted above. Large nucleated erythrocytes have been encountered in certain severe cases of secondary anemia. They may be especially numerous and even exceed the normal size nucleated erythrocytes in severe anemias due to Dibothriocephalus Latus infection, which gives a blood picture identical with that of pernicious anemia, and also in the anemias symptomatic of malignant disease presumably with metastasis in the bone marrow.

Secondary anemia due to lead poisoning differs from other secondary anemias in that the blood smear contains a large number of erythrocytes showing basophilic stippling which is a strking feature of diagnostic significance.

Post-hemorrhagic anemias also show differences from the usual secondary anemias. Immediately after a large hemorrhage the erythrocyte count will be the same as before the hemorrhage, but within a few hours, when the volume of blood is in a large measure restored by means of fluid from the body tissues with consequent dilution of the blood the situation undergoes adjustment; and after one or two days the erythrocytes and hemoglobin fall to a figure proportionate to the amount of blood lost. Active regeneration of erythrocytes begins probably within twenty-four hours and the new erythrocytes are deficient in hemoglobin, which is reflected in the low color index. Some of the new cells show polychromatophilia, and a few nucleated erythrocytes are present, with a moderate neutrophilic leucocytosis. The blood platelets are strikingly increased, even up to one million per cubic millimeter, with increased coagulability of the blood. The normal blood picture is restored in about one month in a previously healthy adult. After a loss of 500 to 600 c.c. of blood, the amount usually taken from a donor for transfusion, the blood picture may be normal again in about one week, although the percentage of hemoglobin is more slowly restored than the other elements.

Under the primary anemias let us consider chlorosis, acute aplastic anemia, hemolytic jaundice, and pernicious anemia.

Chlorosis is an anemia of defective blood formation, confined almost exclusively to girls within the decade following the age of puberty, and is thought to be due to an anomaly of internal secretion of the female sex glands. Incidentally, this disease is now becoming rare. The clinical symptoms furnish the important data for diagnosis but a consideration of the blood findings is essential. There is a marked decrease of hemoglobin with a slight decrease of erythrocytes, giving a strikingly low color index, which may be as low as .3. There is a marked achromia giving a striking ring-like appearance to the erythrocytes. Cells are of uniform size with average diameter a little less than normal. Nucleated erythrocytes are rare. Platelets are increased and the coagulability of the blood is increased. Leukocytes are normal or decreased in number.

Acute aplastic anemia is a rare and rapidly fatal anemia of obscure etiology which appears to be the result of a more or less complete failure of blood formation. At autopsy the red bone marrow is found to have almost completely disappeared, even from the flat bones and the bodies of the vertebrae. The

failure first involves the formation of erythrocytes, then the leukocytes, and finally the blood platelets and, when the platelets become greatly diminished, symptoms like those of purpura hemorrhagica appear. The disease occurs most frequently between the ages of sixteen and thirty, with a duration of about two or three weeks. Stained films show very little of importance. Reticulated erythrocytes are rare and fragility is normal.

Hemolytic jaundice is a rare, chronic, generally hereditary disease, characterized by periods of excessive hemolysis due either to strong hemolytic poisons or to excessive fragility of the erythrocytes. The most striking laboratory finding is markedly increased fragility. The anemia is usually extremely marked, erythrocytes fall as low as 1,000,000 and the color index is .8 or .9. Sometimes the anemia takes on the character of progressive pernicious anemia. The urobilin of urine, feces, and duodenal contents is high. Reticulated erythrocytes may go up to 20 per cent or higher.

Whether pernicious anemia is an entity or whether it represents a group of conditions with similar pathogenesis but different etiology would appear to be a debatable subject. It appears certain that some obscure noxious or toxic agency is responsible for the excessive destruction of erythrocytes and the active abnormal regeneration of erythrocytes by the bone marrow. The nature and origin of the hemolytic toxin however is unknown. Macht[20] has shown that the blood serum of pernicious anemia patients is peculiarly and characteristically toxic for plant protoplasm; and Schultin[21] has shown that the rationale of the liver diet treatment for pernicious anemia, which is yielding such splendid clinical results at this time, is to neutralize this toxin. Ordway and Gorham[22], however, have observed that the underlying pathologic process remains unaffected, and thus, like insulin, the liver diet cannot be considered a cure for the condition for which it is given, although symptoms may be held in abeyance for a protracted period. Since the liver is the great detoxicator of the human economy, it seems reasonable to suppose that pernicious anemia is due to a diminished activity or deficiency in this function of the liver, and that the feeding of liver from a normal animal adds to the body resources this missing substance. This idea would appear to gain strength with recent demonstrations that a liberal, balanced, general diet which includes sufficient liver per day, cooked or raw, or a potent extract of liver, is as effective as the original Minot and Murphy diet.[23] The course of the disease and the blood picture vary with the varying rate of blood destruction and with the functional sufficiency of the erythrogenetic islets. As a terminal result, the bone marrow may become exhausted, giving a blood picture similar to that of aplastic anemia. Characteristic of the clinical course is a striking tendency to clinical remissions, either spontaneous or induced, lasting from a few weeks to a few months or even years. The early disappearance of free HCl from the gastric juice when once established persists even when the blood is practically normal and is reported as persistently continuing when improved as a result of the liver diet.

In conclusion, I should like to offer a summary of the blood picture in pernicious anemia. Erythrocytes greatly diminished, color index above one, leukocytes normal or diminished, platelets reduced and coagulation time delayed. The smears show anisocytosis with many macrocytes, and a few nucleated erythrocytes. Achromia is absent but polychromatophilic erythrocytes showing basophilic granular degeneration are numerous. The reticulated erythrocytes range between 1 and 5 per cent and may go as high as 20 per cent. This is a useful index as to the activity of blood regeneration and they are seen to steadily rise as a remission begins or the liver diet is begun. The fragility is only slightly increased, indicating that excessive hemolysis is not due to increased fragility of the erythrocytes as in hemolytic jaundice.

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THE SYMPTOMATOLOGY AND DIAGNOSIS OF THE ANEMIAS.*

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A thorough understanding of the symptoms and signs of anemia will often aid us in making a diagnosis of many obscure conditions. Anemia may so alter the physiology of various organs that the symptoms produced may simulate many organic diseases. For instance, the cardiac symptoms may be confused with primary heart disease, or the gastric symptoms of pernicious anemia with cancer of the stomach.

For convenience in discussing the symptomatology and diagnosis, the anemias will be arranged in three groups. In Group I are the anemias due to mechanical blood loss; in Group II, those due chiefly to defective blood formation, and in Group III, those due chiefly to increased blood destruction.

The changes which occur in the tissues due to anemia produce a chain of symptoms which may occur in any of the various types of anemia. These vary according to the duration, the character and the intensity of the anemia. In the skin there is usually pallor, although in the lesser grades of anemia the skin may not be pale, while in the severer grades pallor may be overshadowed by jaundice or pigmentation. Lassitude and general muscular weakness are probably the most outstanding symptoms of anemia. The general weakness is a result of a diminished supply of oxygen to the tissues, and effort, either physical or mental, induces varying degrees of fatigue, depending upon the amount of reduction in hemoglobin or in the red cells. An individual with a hemoglobin above 60 per cent can usually carry on his daily duties without marked discomfort, but when the hemoglobin falls below 60 per cent sustained effort is difficult. There are certain symptoms which may be classed as follows: First, those referrable to the gastro-intestinal tract, such as nausea, vomiting, fullness, epigastric pain, constipation or diarrhea. These are very prominent in pernicious anemia. Second, those pertaining to the cardio-vascular system such as, shortness of breath, tachycardia, precardial pains, palpitation, which may be the patient's chief complaint. Third, the symptoms from the central nervous system, as headache, insomnia, drowsiness, excitability and vertigo may be present. In addition, other symptoms may occur in anemia, as elevation of temperature, tendency to hemorrhage, amenorrhea, edema, low specific gravity of urine, and albumin. The symptoms and signs peculiar to each individual type of anemia will be discussed under the diagnosis.

The diagnosis of diseases of the blood and blood forming organs in many instances is very simple, while in others it is one of the most difficult problems in medicine. A carefully taken history, a thorough physical examination and complete examination of the blood are necessary in arriving at a diagnosis.

I. Anemia Due to Mechanical Blood Loss

Anemia due to mechanical blood loss may be acute or chronic.

The diagnosis of acute anemia due to blood loss is usually made from the history, and clinical picture. Immediately following acute hemorrhage when considerable amount of blood is lost the red cell count is normal, but within a few hours as the blood volume is being restored the red corpuscles and hemoglobin show a reduction while polymorphonuclear leucocytes are increased. The blood pressure in acute hemorrhage is low, and a continued low systolic pressure is indicative of persisting hemorrhage.

Acute concealed hemorrhage may be confused with shock. However, the history and physical findings will usually establish the differentiation.

The diagnosis of chronic anemia due to blood loss is usually obtained from the his-

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tory and the finding of the condition responsible for the hemorrhage. The blood examination will show varying degrees of anemia with increased bone marrow activity. Although in prolonged or repeated hemorrhage the bone marrow activity may be diminished, and the blood findings are similar to those of pernicious anemia, the typical histological cells and the increased blood destruction of pernicious anemia do not occur in chronic hemorrhage.

Anemia due to chronic hemorrhage is sometimes associated with abnormalities of the blood, as in purpura hemorrhagica, which can be determined by a complete study of the blood.

II. Anemia Due Chiefly to Defective Blood Formations

The anemias due chiefly to defective blood formation are numerous. A study of the blood will show varying degrees of anemia with normal or diminished bone marrow activity. Some of the anemias of this group may show slight evidence of increased blood destruction, but the predominating feature is aplasia.

Simple anemia due to defective blood formation is the most frequent type met in general practice. The causes are numerous, the most frequent of which are intoxication from poisons, such as lead, mercury, arsenic, etc., infections of all types, intestinal parasites, toxemias from the liver and kidneys, deficient diet and lack of outdoor exercise. The symptoms the patient may present are usually those of the underlying condition, and the anemia found in the course of general examination may be a factor in retarding the patient's convalescence. The blood findings are varying degrees of reduction in the hemoglobin and red cells, which latter show no special morphological changes.

Myelophthisic anemia is due to a crowding out of the hemopoietic structures of the bone marrow by tumors or tumor-like formations, and the diagnosis is dependent on the finding of the malignant growth with metastasis to the bone, or primary bone tumors, such as myeloma or chloroma. The erythrogenic areas are also crowded out in the leukemias.

Chlorosis, a condition becoming more rare, is characterized by a low hemoglobin, out of proportion to the reduction in the red cells.

Idiopathic aplastic anemia is a distinct blood disease, which is progressive and has a fatal termination within a few weeks or months. In the early stages there is usually a history of increasing weakness for weeks. Sometimes there is a history of infection. These individuals appear pale, and the skin usually has a waxy appearance. In the late stages there are usually petechial hemorrhages or symptomatic purpura hemorrhagica. Examination of the blood shows no evidence of bone marrow activity. The white cells are greatly reduced with an absolute diminution of the polymorphonuclear leucocytes. The platelets are markedly decreased, and often absent. The red cells are very low, frequently below one million. A stained smear shows very little change in their size, shape, or amount of hemoglobin. The reticulocytes and nucleated reds are usually absent. The resistance of the red cells to salt solution shows beginning hemolysis in about the same strength as normal cells, but complete hemolysis is in a higher percentage of salt solution. This type of reaction is very unfavorable. The diagnosis can usually be made from the history and blood findings.

Since there are petechial hemorrhages in aplastic anemia, there may be confusion with true purpura hemorrhagica. But in idiopathic aplastic anemia the petechial hemorrhages occur after the anemia develops, while in purpura hemorrhagica the petechial hemorrhages precede anemia.

III. Anemia Due Chiefly to Increased Blood Destruction

The hemolytic anemias are characterized particularly by increased blood destruction, although some of these may also show defective blood formation. In certain instances many of the hemolytic anemias may terminate in aplastic anemia.

During certain periods pernicious anemia produces symptoms and signs referable to more structures or organs than any other form of anemia. General muscular weakness is one of the most prominent complaints. In the early stages there is usually a history of sore mouth, nausea, and recurrent attacks of diarrhea. The free HCl is most often absent. The skin shows varying degrees of light jaundice, and the spleen is usually enlarged. As the disease progresses the symptoms referable to the cardio-vascular and central nervous sys-

tems may be marked. The blood examinations show evidence of increased blood destruction, with megaloblastic regeneration. The diagnosis should be made from a thorough study of the blood interpreted in the light of the history, and physical examinations.

The differential diagnosis of pernicious anemia during certain stages is very difficult. The gastro-intestinal symptoms may resemble those of cancer of the stomach, but a negative X-ray finding and complete study of the blood will establish the diagnosis of pernicious anemia. The history and blood findings of pernicious anemia do not occur in primary heart disease. Aplastic anemia and other hemolytic anemias each have their characteristics.

Acute hemolytic anemia occurs most frequently in sepsis, malaria and pregnancy. The skin is jaundiced, and there is usually enlargement of the spleen. The diagnosis is dependent upon the finding of the condition producing the hemolysis.

The chronic hemolytic anemias may be acquired or congenital.

The chronic acquired types are produced in the same manner as the acute hemolytic forms, but the course is less severe. The most frequent causes are syphilis, fish tapeworm, cancer and pregnancy.

Chronic congenital hemolytic jaundice represents one of the purest types of excessive blood destruction. The clinical aspects are familial tendency, mild course, jaundice, enlarged spleen, mild exacerbations, diminished resistance to salt solution, and usually associated gall-stones.

In summarizing this sketchy review of the large domain of anemia, one is justified in the light of present knowledge in arriving at the following conclusions: First, the anemias are due to mechanical blood loss, defective blood formation, or pathological hemolysis. In so-called primary anemias, defective bone marrow physiology and abnormal internal blood destruction probably are associated etiological factors, but in each group one or the other predominates. Symptomatically, all the anemias behave alike in so far as their symptoms are due to anoxemia. However, the entire clinical picture varies according to the basic etiological factor on the one hand, and the associated somatic changes on the other. The diagnosis should not depend upon any single factor, but upon a careful consideration of the history, physical examination, and thorough study of the blood.

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THE MEDICAL TREATMENT OF THE ANEMIAS.*

By J. C. FLIPPIN, M. D., University, Va.

Owing to time limitations, these remarks on the treatment of the anemias will be limited to one specific disease—primary pernicious anemia—and another group (to be more definitely defined later), some of the more frequently encountered secondary anemias.

Pernicious Anemia

It may be stated without reserve or hesitation that the treatment of pernicious anemia with liver substance is one of the most brilliant medical achievements of our day. Recently published papers and discussions have so fully and admirably summarized the present state of our knowledge in this subject that the reviewer finds it difficult and even embarrassing just at this time to make further interpretations. Certainly, I should not attempt it except as an assigned task.

Reports of the results of treatment of pernicious anemia with mammalian liver and liver extracts are singularly unanimous in all essential details. There is available a series of cases sufficiently large to bring conviction to the most skeptical. The major observations have been carried forward under conditions so carefully controlled as to make this work an eloquent tribute to modern scientific methods.

The outstanding fact is that if a patient with pernicious anemia during the period of relapse is fed approximately one-half pound of liver a day, about 230 gms., or a potent extract from 400 to 600 gms. of this liver, the blood will quickly assume or approximate the appearance of that of a normal individual and the patient will be correspondingly relieved of the more usual and distressing symptoms of the disease. This epoch-making contribution to medicine we owe to Dr. George R. Minot, of Boston, and his coworkers, who in turn were directed to the problem by the experiments of Dr. George H. Whipple and associates. Whipple had announced the observation that anemia produced in dogs by repeated bleeding was very favorably influen-

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ced by the addition of liver and kidney to the diet. Minot, impressed with these observations, gave the liver diet a thorough going trial under carefully controlled conditions with the result with which we are now familiar. Now that clinical experience has thus far demonstrated the relatively small and uncertain value of liver diet in ordinary cases of secondary anemias, including those resulting from hemorrhage, its marvelous and specific action in pernicious anemia is seemingly a strange paradox.

The typical and almost invariable effect of liver therapy is as follows: From a level of 1 to 3 per cent there is a delivery of young red cells—reticulocytes—into the peripheral circulation amounting to 5 to 6 per cent within three to five days, reaching a maximum of 10 to 30 or sometimes 50 per cent in about ten days, falling again by the fifteenth or the twentieth day. The red cells show a prompt increase, frequently an addition of two and a half million in thirty days. The hemoglobin percentage rises more slowly, but eventually approximates a normal reading. The icteric index falls and the yellow color of the skin disappears. The morphology of the blood gradually returns to normal as macrocytes, microcytes and polychromatophilia disappear. The leucocytes rise with increase in polymorphonuclears and eosinophiles. Platelets also increase in numbers. The patient is symptomatically improved with the change in blood picture.

Patients who have maintained the diet have now sustained this remission for three years or more. When liver is omitted there is a gradual relapse to former condition. A return of free hydrochloric acid to the gastric juice has been reported in only a few cases. Rather strangely I think the administration of hydrochloric acid is said not to be of value, but further evidence is desirable on this point. Well marked evidence of involvement of the central nervous system (most commonly combined sclerosis) usually remains unchanged, although the early symptoms may disappear or show improvement. The records of some five hundred to a thousand carefully studied cases are available and the results reported are surprisingly uniform.

Properly prepared liver extract in adequate dosage has essentially the same beneficial effect as liver substance. Perhaps the hemoglobin increase is not quite so rapid unless iron is supplied either in the food or in the inorganic form. The extract used in most cases reported is that prepared by the Eli Lilly Company under supervision of the Pernicious Anemia Commission of the Harvard Medical School. The active principle of liver affecting the course of pernicious anemia is soluble in water, insoluble in ether and precipitable by alcohol. It is thought to be either a nitrogenous base or a polypeptid. This particular preparation is now being marketed by the Lilly Company as preparation No. 343. It is a yellowish powder, soluble in water and when given in doses of about .6 gm. a day produces the characteristic response of reticulated cells.

The extract naturally has many advantages over liver feeding. Many people do not like liver and it is apt to pall upon the taste when eaten every day for months and years. Furthermore, it cannot be regularly supplied in rural districts.

It is already apparent that precautions must be used in the preparation of the extract as relatively inactive lots have been encountered. It should also be borne in mind that a fertile field for commercial exploitation has been opened and only those extracts should be relied upon which have been carefully standardized.

Minot and Murphy report no effects from liver or liver extract on the blood of the normal individual. Recently, Berglund, of Minnesota, reports that he has produced an increase of red cells and hemoglobin at least temporarily in the normal subject. This investigator also finds greater potency in the liver substance of fetal calves in certain secondary anemias than from the livers of adult animals. This, of course, is suggestive but needs further study.

Secondary Anemias

In comparison with these clear cut and most satisfactory results from liver extract in pernicious anemia, the question of the effect of liver substance on the secondary anemias is at present very much in the air. The reported cases of Minot and Murphy would indicate that its field of usefulness in anemias other than the pernicious form is quite limited. As against this we have the evidence of Whipple that liver has an appreciable effect upon the anemia of laboratory animals after hemor-

rhage. This experimental evidence is supported by the experience of others. Clinical reports are exceedingly variable and at present hard to interpret. The anemia caused by the fish tape-worm—dibothriocephalus latus—and which closely resembles pernicious anemia morphologically, admittedly reacts very much as does pernicious anemia. Certain anemias arising during pregnancy of obscure origin have been reported as being materially benefited. In fact, isolated cases of many varieties of anemia are said to have responded favorably to liver diet. On the whole, however, it would seem that this method of therapy cannot be thought of at the present time as being specific for the secondary anemias. We are, therefore, not justified in relying upon liver treatment in such anemias, certainly to the exclusion or neglect of other measures.

A very large percentage of secondary anemias we are called upon to treat are due either to hemorrhage, bacterial infection, parasitic infestation, toxemias resulting from diseases, such as nephritis, cirrhosis of the liver, malignancy, or to defective nutrition. This list by no means exhausts the causes of secondary anemia, as will be readily seen, but are to be thought of as the causes most frequently operative in this part of the world.

Assuming that we have done our full duty in patiently searching for and as far as practicable removing the cause in a given case, what further measures are available in treating the anemia? When we are confronted with sudden and considerable blood loss, or a very severe type of anemia from other cause (with the exception of the pernicious type), or a chronic anemia which has resisted other methods of treatment, unquestionably the most prompt and efficient measure for relief is blood transfusion. The idea of transferring blood in some manner, either from the lower animals to man or from one human being to another had its birth in the very earliest era of medical history. No attempt will be made either to trace the historical development of blood transfusion or to discuss in adequate fashion the present day status of this therapeutic measure. However, in view of the importance of blood transfusion in the anemias and the growing frequency of its use, at least brief mention must be made of some of the principles involved.

Blood transfusion as a relatively safe and practical therapeutic measure is largely dependent upon the more exact knowledge of the phenomena of iso-agglutination and hemolysis developed in the first decade of the present century, coincident with improved technical methods and larger experience in and about the period of the World War. Human healthy blood is, of course, an ideal substance to introduce into the circulation of a patient having blood deficiency. The plasma fulfils physiological demands more fully than any fluid yet devised, although in emergencies blood volume may be temporarily restored by physiological saline solutions. It has been definitely proven that the transfused red blood corpuscles will function in the body of the recipient and that the life of the individual cell is of considerable duration. Records on this latter point are somewhat conflicting, but it would seem safe to assume that in properly matched cases red cells will live forty to sixty days and carefully controlled experiments have indicated an even longer period of life.

When done under proper precautions it may be said that blood transfusion, while not without some danger of unfavorable or even serious reaction, is a relatively safe procedure. In experienced hands whole blood transfusions are not technically difficult and if an anticoagulant is used, the whole procedure is a relatively simple one, even for those of small experience.

In our very proper enthusiasm we should always keep in mind the dangers involved, some of which we do not yet fully understand and others can be obviated only by utmost vigilance. It cannot be too strongly emphasized that careful matching of the blood of the donor with that of the recipient should always be done immediately before transfusion. Persons having blood of type IV of the Moss classification are, of course, much more favorable subjects, either as donors or recipients, but it should not be overlooked that intercurrent infections and probably other causes may temporarily change the agglutination reaction in any individual blood. Donors should preferably be young, reasonably vigorous individuals and proven free of transmissible disease, particularly syphilis.

The ideal method undoubtedly is the delivery of healthy unchanged blood directly into the circulation of the patient. At present the technical difficulties of accomplishing this have

not been altogether overcome, certainly for those who are only occasionally called upon to perform transfusions. In the hands of those especially trained it would seem to be the method of choice. The citrate method being far simpler for the average person, the question is a natural one as to whether the citrate method has any real objections as compared with other methods. I think it may be fairly stated that in the concentration used, about .2 of 1 per cent. sodium citrate does not lengthen but apparently shortens the coagulation time *in vivo*, a point which would, of course, arise in transfusions for hemorrhage of various causes. It is said to have the disadvantage of increasing the fragility of red cells, it reduces the opsonic index of the plasma and the phagocytic power of the leucocytes. Some observations indicate that it causes a disintegration of platelets and destroys complement. All of these effects are probably relative and it is still a question whether the effect of citrate in this and other possible ways is sufficiently powerful to make it a practicable objection.

What of dosage? It is well to remember that the total blood volume is about 5 per cent of the body weight of an individual, which in the average adult would be about 4 litres; for an infant of 7 lbs. about 160 c.c. Clinical opinion varies somewhat widely as to optimum dosage. As much as 2,500 c.c. has been given to adults in extreme cases. On the other hand some advise small amounts, 5 to 10 c.c. daily. The usual custom is to give about 400 to 700 c.c. at a time and this can be repeated at intervals of one to two weeks when necessary. Infants and children receive amounts proportional to body weight.

Donors must also come in for some consideration. While it has been shown that the body will withstand the loss of one-third of the total blood volume, which in the adult would be 1,200 to 1,500 c.c., without untoward symptoms, it is wise to keep well below this limit. A vigorous, healthy individual will usually have no ill consequences from the loss of 500 c.c. Many professional donors have given enormous quantities of blood over periods of five or six years. However, experience indicates that well marked anemia may result from too frequent donations; 500 c.c. at intervals of four to six weeks is perhaps conservative. It should be remembered that blood is toxic in direct proportion to the chemical alterations toward coagulation, therefore speed is of great importance when anticoagulants are not used, and careful mixing and avoidance of coagulation is imperative in the citrate method.

In repeated multiple transfusions, sensitization may occur, as in the administration of horse serum, but such cases must be rare and can be avoided by desensitization. In infants before closure of the fontanelle, transfusion has frequently been done into the longitudinal sinuses. In older children the veins of the neck are practicable avenues. Recently, excellent results have been reported in children, particularly by Grulee, based upon the experiments of Siperstein and Sansby, through the use of intraperitoneal injections of citrated blood. Apparently the corpuscles promptly pass into the blood stream and function as in intravenous introduction.

Radiant energy probably deserves some mention in any discussion of the treatment of anemias. Radiation from the quartz mercury lamp and other sources of radiation have been shown to have definite effect upon the blood. In long exposure these rays appear to cause anemia. In lesser dosage a number of investigators have reported a stimulating effect upon blood production. Direct sunlight at least is usually available and the influence of heliotherapy in anemia certainly deserves attention and will doubtless receive further study.

What can we say of the efficiency of drugs in the treatment of anemia? The two drugs most commonly employed are arsenic and iron. Although widely used in various types of anemia for many years, there is reason to doubt whether arsenic has a direct effect upon blood genesis, maturation or hemoglobin formation. The view is generally accepted that arsenic has a stimulating effect upon metabolism in general and individuals suffering from secondary anemia of the type under discussion may be indirectly benefited. The most obvious pharmacological action of arsenic is its effect upon the capillaries, where dilatation is produced. This may well have an effect upon nutrition and metabolism. The well known Fowler's solution has maintained its popularity for oral administration, while the combination of arsenic with cacodylic acid is usually favored for the hypodermic route.

Iron still maintains the position as the one

most useful drug in the treatment of the secondary anemias. In recent years doubt has arisen as to the beneficial effects of iron therapy. Although admittedly no panacea, both clinical experience and much experimental evidence support the view that iron has a very definite place in the treatment of the anemias. The following statements, briefly expressed, seem justified. Iron depletion occurs particularly in the anemias secondary to hemorrhage to defective diet or faulty assimilation. It does not occur characteristically in the hemolytic types of anemia, as in cases resulting from certain infections and toxemias. Here much of the iron is stored after the destruction of the red cell, particularly in the liver and spleen, and is there held available for hemoglobin formation. The total iron content of the body is small, but it may be remembered that a high caloric diet, particularly when largely composed of milk, butter and wheat flour, may not supply requisite amounts of iron for body requirements.

The inorganic preparations, those which have been used for years, such as ferrous carbonate, reduced iron, saccharated iron, appear to be more effective than any organic compound yet devised. Large doses sometimes produce results when small ones are ineffective. Iron is often not well borne by the stomach. For this reason and possibly others, hypodermic or intramuscular administration has a certain degree of popularity, the green citrate being usually employed.

Recent investigations, particularly those of Whipple and his co-workers, indicate that certain articles of food have a specific effect upon the efficiency of iron administration. Whipple found that not only liver and kidney, but other glandular organs, as well as fruits, such as apricots, peaches, raisins and apples, given to dogs rendered anemic by repeated bleeding greatly enhanced the action of the iron. These and other studies strongly indicate that we haven't by any means solved the problem of iron therapy.

It has been suggested that there is a radical in the hemoglobin molecule which cannot be built up in the body and this can be derived only from food. If the diet is deficient in such foods anemia results in spite of iron administration. The vitamins have been thought of as being directly concerned with the production and consequent cure of anemia, but this view is as yet unproven. In general it may be predicted that in the immediate future foods will receive far more attention in the problem of anemia than they have in the past.

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SURGERY OF THE ANEMIAS.*

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The splendid papers already presented in this symposium on "The Anemias" leaves very little to discuss from a surgical standpoint in the treatment of these conditions. I think I can safely rule out of this discussion all those secondary anemias which are of chronic nature and due to specific causes, such as bleeding hemorrhoids, bleeding fibroids of the uterus, etc., and also include in this category purpura hemorrhagica for in this disease the anemia is always secondary and dependent upon the bleeding which is produced by some unknown cause.

Proceeding at once to the point, I think it is wise to say that specific surgery for the anemias must center around the spleen and, therefore, I feel that the premises of this discussion should cover the following conditions:

1. Splenic anemia.
2. Hemolytic jaundice.
3. Gaucher's disease.
4. Pernicious anemia.

It is a fact that we frequently have a chronic type of anemia due to certain chronic infections in the spleen, but I feel that this belongs distinctly to a field covered by indications for splenectomy and not in this particular discussion.

Since the surgery of the anemic conditions

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mentioned above center around the spleen, it would seem appropriate that this paper cover some of the salient factors that relate to the removal of the spleen.

The role of the spleen in the human physiology is not known nor is its necessity demonstrated. This is the first premise in considering the indications for splenectomy. Surgeons should be honest enough to admit that, as far as their knowledge goes, the spleen appears to perform no function of sufficient importance to weigh against its removal. In contrast to the negative influence on the human from the removal of a normal spleen, the removal of a diseased spleen often provides a definite opportunity in certain conditions for improvement to the individual. Physiologists tell us that the normal spleen conveys about 30 per cent of the total blood of the body to the liver, and thus we can readily see the enormous pathological possibilities that must necessarily be inherent in a diseased spleen.

Most surgeons today are inclined to the belief that the spleen does not have the power or ability to initiate primary pathological processes but that the organ acts as an agent secondary to pathological processes initiated elsewhere; and that, therefore, when considering the normal function of the spleen we can readily see how, if this function is deranged, the pathological spleen may become a serious menace to the constituents of the blood and to the normal functions of the liver.

In order that the surgeon may formulate an intelligent opinion as to the necessity of splenectomy, it is important that what we know of the functions of the spleen should always be kept in mind. Speaking in a broad way, the main function of the spleen is shown in its effect on the blood, and this, briefly, may be noted under three headings: first, destructive action upon the red blood cells; second, a strainer or separator action by which organisms are removed from the blood stream and sent to the liver for destruction; third, the formation of lymphocytes. In considering the first of these functions, namely, destruction of the red blood cells, we immediately connect with splenectomy the three types of anemia,—hemolytic icterus (which is not a true anemia), pernicious anemia and splenic anemia.

I think I shall not be considered radical if I devote only a brief word to the consideration of splenectomy in pernicious anemia, for the operation in this disease does not appear to be based on sound reasoning and at the best promises only a remission of the symptoms for a brief period of time. When pernicious anemia has developed to the stage where the blood is characteristic it is an incurable disease, but splenectomy in some instances may offer a decided palliation. Many of these cases in the early stage do not show the characteristic symptoms of pernicious anemia; it is in these cases splenectomy offers the best hope for cure or considerable palliation. In elderly individuals the operation should never be considered, but in the middle-aged and young, if the disease is progressing rapidly and hemolysis is a marked symptom, splenectomy should be undertaken as a last resort.

Liver Diet

In the last two years the result of liver feeding in cases of pernicious anemia has made it seem justifiable to not only rule out the necessity of transfusion in these cases but also to make it thoroughly unwise for the surgeon to consider splenectomy. Accordingly, the above remarks relating to splenectomy are entirely academic, but this discussion on the surgery of the anemias would be incomplete without the presentation of the results relative to splenectomy in pernicious anemia which have preceded the advent of liver feeding.

In the consideration of splenectomy for splenic anemia, we find that the results are very much better in contrast to the failures of this operation in pernicious anemia. It is true that in splenic anemia we are not dealing with a definite clinical entity until possibly the last stages of the disease and the great difficulty in choosing the operation of splenectomy lies in adapting it to the clinical entity of splenic anemia. Most of the confusion arises in differentiating between portal cirrhosis or biliary cirrhosis, both carrying with them enlarged spleens, and the chronic form of splenic enlargement with a secondary anemia which characterizes the syndrome of splenic anemia. In splenic anemia unassociated with cirrhosis in any form, splenectomy has proven very favorable, resulting in about 60 per cent of cured cases. The results are not always immediately encouraging for often the anemia is exaggerated over a period of four to twelve weeks.

Gastric hemorrhage is not always relieved by splenectomy and the recurrence of gastro-

XUM

intestinal bleeding may follow. Some of these recurrences are often and extend over a long period of time, but usually they are rare and, if occurring at all, show themselves only a few times in the recent months following operation. The relief of the hemorrhage depends in part upon the condition of the liver and especially upon the amount of portal cirrhosis in the liver. Because of the large amount of blood carried through the spleen, the total circulation in the liver is relieved of a large portion of venous blood by splenectomy, but if there is considerable portal cirrhosis, with accompanying venous obstruction, associated varicosities of the esophagus or gastric mucous membrane, or superficial gastric erosions, we may readily understand how splenectomy cannot be expected to relieve the recurring hemorrhages in this type of case. It is well for us, therefore, to remember these contingencies in estimating the value of splenic removal for advanced pathological changes associated with splenic anemia.

There are two types of anemias occurring in childhood which are classified under the names of Gaucher's disease and von Jaksch's anemia. Both conditions seem to be clinically the same and the only differentiation is finding, in Gaucher's disease, the large vesicular cells which fill up the splenic sinuses. These two conditions in children simulate to some extent the splenic anemia of adults and it is well before passing from the subject of splenic anemia for us to consider the results of splenectomy for this condition in infancy and childhood. It would seem that most excellent results have been obtained even in the severe type of the disease in children, and I have been able to find reports covering seventy-two children under fourteen years of age who were splenectomized for splenic anemia with a resulting cure or marked improvement in thirty-six of the cases.

I believe that it is the general opinion of experienced surgeons today that splenectomy in children for the present should be reserved for the more severe type of cases. Improvement follows medical treatment in the milder types, but children with the more severe types usually die of some intercurrent infection unless operated upon before this infection occurs. The association of a biliary cirrhosis with a hemolytic icterus is a common condition, and this is probably due to the widespread destruction of the red corpuscles in the spleen, which in the broken down state are carried to the liver as blood pigments, and these in turn render the bile thick and viscid in character. Thus the flow of bile in the biliary portals is sluggish, so that congestion and inflammation around the bile passages readily occur with a disposition of fibrous tissue. The appearance of gall-stones associated with hemolytic icterus is very frequent and quoted by some authorities in about 70 per cent of their cases. We may thus see how easy it is to confuse the diagnosis of biliary cirrhosis, associated with gall-stones, and hemolytic icterus. On account of the exaggerated function or ability of the spleen to destroy the red blood corpuscles, which is so marked in the condition of hemolytic icterus, we can justly appreciate the reason for the excellent results that follow splenectomy in this condition, and splenectomy in hemolytic icterus is the operation of choice. There is no operation in surgery that is followed by more brilliant results than splenectomy for hemolytic icterus unless done in the terminal stage. It is only cases in the terminal stage, pathologically, with marked cirrhosis of the liver and secondary gall-stone formation that fail to be relieved by the operation. Care, however, should be exercised in not operating on these cases during a temporary exacerbation of their symptoms characterized by an increase of the jaundice, fever, marked tenderness and increase in the size of the spleen. These characteristic crises are usually temporary in character and operation should always be deferred until the decline of the more active symptoms.

In conclusion, I think it would be conservative to say that there is a definite field of usefulness for specific surgery in certain types of the anemias. It is, however, well to bear in mind that these are not primarily surgical conditions in which to exploit surgical efforts and that only through careful co-operation with an internist can the surgeon hope to properly select his cases for operation and at the same time escape many of the blunders of a too eager decision which has occurred so many times in the past, as recorded in the medical literature on splenectomies.

Medical Arts Building.

DISCUSSION OF PAPERS BY DRS. BECK, NOFSINGER, FLIPPIN AND PAYNE.

DR. F. C. RINKER, Norfolk, Va.: I am sure I express the feeling of everyone here when I say that I regret that Dr. Martin is not present and also that we regret his illness. He has probably had an opportunity, I am sure he has, to work up a discussion after rehearsing these papers. He has been particularly interested in the treatment of the anemias and in the separation of the secondary from the primary anemias, regarding therapy.

I am going to take up each paper. I have nothing, certainly, to discuss, but everything to sanction and agree with; but there are some points I think might well be stressed.

Dr. Beck's paper very well brought out the importance of determining hemoglobin in percentage rather than the reading of it on some standardized scale, and she told us of how much more value it is to determine hemoglobin in grams per 100 c.c. of blood than it is to make our standardized reading. I think we should also keep in mind the physiology, as described by Dr. Beck, when we are attempting to differentiate secondary from primary anemia. It is not always easy, but if we keep in mind a graphic description of the erythrogenic center I think we shall realize that in the center of a graphic drawing there would be the young cells and at the periphery the adult cells, and as the adult cells are called upon and destroyed, then the young cells are thrown into the circulation.

Dr. Nofsinger, in his paper on the symptomatology, gave us a very good classification. The only thing I wish to say here is that many of the hemolytic types are difficult to differentiate. I also wish to call attention to one pitfall that I think he overlooked, and that is the frequent mixing up of primary anemias (so-called pernicious anemia), with the aleukemic leukemias. Many times I think we have been at fault in making a diagnosis of primary anemia when dealing with this type of leukemia. He did not suggest some of the more severe neurological findings, such as paresthesias and the ataxias, which are found late in the disease.

Coming to discussion of Dr. Flippin's excellent paper, I simply wish to stress this point, that liver extract is definitely of value in primary anemia, and probably not valuable at all in secondary anemias. I might, however, say possibly instead of probably, because some of the secondary anemias will probably fall into the class that is amenable to treatment with liver. In my experience I have found that liver is of greater value than liver extracts. Dr. Flippin told us that we must be careful in our selection of liver extracts. This is important.

One important thing Dr. Flippin stressed is typing of the donor's blood immediately before it is used. I think probably sometimes we have used a donor ten days or two weeks later who typed perfectly during the first use of his blood; may be we have used that donor without retyping. There we have run a tremendous risk.

Dr. Payne has described the surgery of the anemias as well as it can be done. Splenic anemia and hemolytic icterus definitely fall into the class of surgical lesions. Gaucher's disease and von Jaksch's anemia probably fall into the surgical conditions, but he has said in his conclusions that these cases should be operated upon as soon as they are definitely determined to be surgical and not medical conditions. With this I heartily agree.

DR. SEALE HARRIS (Invited guest), Birmingham, Ala.: The term "primary anemia" will have to be given up in discussing pernicious anemia, because it seems probable that pernic ous anemia is secondary to some liver pathology. We think that it is secondary to a hepatitis that may have occurred years before the anemia developed and that the cause of pernicious anemia is a deficiency of an endocrin that controls erythrocytolysis. In other words, the equilibrium of five million red blood cells per cubic millimeter is maintained by the regular destruction of the red cells by the reticulo-endothelial cells, the Kupffer's cells that are in the liver and spleen and bone marrow. There is something that controls the action of those reticulo-endothelial cells. Perhaps the liver secretes this endocrin, and when the liver is diseased or those cells are destroyed or their action inhibited there is not enough of this inhibiting substance secreted and there is excessive destruction of red blood cells. If this were so, an excessive secretion of this antihemolytic endocrin would result in polycythemia; and Joslin states that in Strassburg, where pate de foie gras and liver sausages are manufactured, pernicious anemia is unknown, but polycythemia is frequent. In other words, the excessive ingestion of liver supplies too much of the endocrin that inhibits erythrocytolysis, and polycythemia results. In every case of pernicious anemia the essential pathological finding is of the liver, a previous hepatitis. Often there is an association of gall-bladder infections with the borderline anemias, and cholecystectomy improves or cures the anemias. Surgeons have observed that in the chronic cases of cholecystitis there is an associated hepatitis, and perhaps such cases are potential pernicious anemias, and the removal of the gall-bladder may prevent the development of the anemia. We think that there is strong evidence that pernicious anemia results from a deficient secretion of a liver endocrin and that therefore it is a secondary disease.

DR. W. LOWNDES PEPLE, *Richmond:* A young married woman of twenty-three was brought to me in March, 1928, complaining of enlarged spleen and anemia. It was thought that she had chronic malaria, and she had been treated extensively for it during the past eleven years, though she had never had chills and fevers and the parasites had never been found in her blood. She was transferred to the medical department for study. It was found that her mother and two of her sisters also had big spleens, were chronically anemic, and of yellowish complexion, though not frankly jaundiced. The patient herself was definitely jaundiced on admission, and the icterus index was 20. Her hemoglobin was 50 per cent with the Dare instrument, and the red blood cells were 2,600,000. The fragility test showed that her red blood cells were hemolyzed much more readily by hypotonic saline solution than are normal cells, and the reticulated red cells in the blood smear were 22 per cent. A diagnosis of familial hemolytic icterus was made. In addition to this condition it was found that she was about three months pregnant. It was decided to send her home for a month of rest in bed on iron, arsenic, and liver in an effort to build up her blood so the splenectomy might be done with less risk. She returned at the end of the month in worse condition than when previously seen. The hemoglobin had fallen to 40 per cent, and the bed blood cells to 2,200,000. It was decided that longer delay was useless, so on April 11th an abortion was done, and during the next two weeks the patient was put on large doses of liver extract and given three transfusions of whole blood of 500 c.c. each. Her blood count the morning of operation was hemoglobin 72 per cent,

XUM

red blood cells 4,000,000. A spleen was removed which weighed about 1500 grams, about ten times the size of a normal spleen. The patient reported three months later for check-up, and it was found that her hemoglobin was 78 per cent, red blood cells 4,600,000, the icterus index was only 5, both the direct and indirect Van den Berg gave negative reactions, and there was no urobilin in the urine. The fragility test was normal, and the reticulocytes in the blood smear were only 0.5 per cent. Clinically, the patient was an entirely different person and stated that she had felt better and stronger than she could ever remember having felt before.

DR. WILLIAM H. HIGGINS, Richmond: Among the complications of pernicious anemia I suppose the one that stands out with greater prominence is that of cord change, and although these changes are not exceedingly common probably all of us see from one to three or four every year as complications in this form of anemia. Unfortunately, there is no indication from the degree of anemia as to the likelihood of involvement of the cord, for there are instances where evidences of posterior lateral sclerosis have preceded other signs and symptoms of pernicious anemia. In other instances it has followed, indicating that neither one is the cause of the other but that probably both are caused by the same toxin that has gotten into the system. The pathology of advanced posterior lateral sclerosis is so definite that one studying sections of the cord of a person dying of the disease could see that any marked improvement would be very unlikely. The writings of Minot and Murphy and circulars sent out by Lilly with liver extract, state that no improvement is likely where there are these cord changes and also state that there are no instances where cord lesions have developed during the course of liver treatment. Only recently Dr. Rupert, of Baltimore, in *The Journal of the American Medical Association*, has cited one case that came to him with very definite signs of cord changes, with marked ataxia, necessitating the man's using two canes, and all the definite signs of a well marked sclerosis. After liver feeding for one year the man was able to walk and attend to all his duties and uses now only one cane, probably from habit rather than from real need, showing that we can hope in some cases for marked improvement.

Only recently another physician reported a case which in the course of the treatment of the disease developed marked signs of a posterior lateral sclerosis. I should like to add to that a case which I saw in consultation with Dr. Fuller, in Danville here, about a year ago; a well marked case of pernicious anemia with a blood count, when we first saw him, of red blood cells 2,300,000 and hemoglobin of 30. He was started on liver extract, the blood improved rapidly, and he gained thirty pounds. He was still using liver. I saw him again last April, and while he had held his weight and his blood had shown no remission, yet he could walk only with the greatest difficulty. He was using two canes and had all the sensory signs of a cord lesion. I had a letter recently from Dr. Fuller saying the man was in bed and had lost sphincter control and had all the signs of the final stages of a sub-acute sclerosis. This was a rather remarkable instance of extreme cord changes occurring during the feeding of liver extract.

DR. J. POWELL WILLIAMS, Richmond: My experience has been entirely different from the results reported by Dr. Higgins and many others using liver therapy in the neurological lesions of pernicious anemia. I have had in the last eighteen months five cases of subacute combined degeneration, none of whom was able to walk at the time of admission to the hospital. One was the flaccid type with absent reflexes, just as in tabes dorsalis. The other four were of the spastic type with marked evidence of pyramidal tract involvement. There is not a single one of these cases who is unable to walk at the present time. The most recent one is using one cane; the other four walk without assistance. Two are farmers, and they have returned to nearly full-time work in the fields. They are forbidden to attempt the more difficult work, but are able to do a great deal. All of them show some evidence of their disease, such as positive Romberg and walking with a wide base. The vibration sense has not returned in any of them, though the pyramidal tract signs have disappeared in the four who showed them. Subjective sensation of numbness and tingling has been markedly reduced in all but is still present to a greater or lesser degree.

There is one thing that might account for the difference in the results I have gotten and those reported from the use of whole liver feeding. Patients having to take large amounts of liver every day over long periods of time usually become very tired of it, reduce the amount below that which is necessary for therapeutic results, and frequently stop it altogether. We have used liver extract in doses which were equivalent to one and three-quarters to two pounds daily. It can be given in palatable form between meals, so as not to interfere with the daily menu. It costs the patient nothing at the present time, which is a considerable attraction to the poor patients. We use the liver extract as bait to get the patients back for frequent observations and encouragement in the continuance of its use. Until definite improvement occurs they are seen every two weeks, and later the intervals are lengthened to once a month.

Dr. Higgins states that the lesion in the cord in this disease is a diffuse sclerosis from which little improvement can be expected. Long, James Collie, and Sir James Purves Stewart, along with all the more recent investigators, state that the distinguishing feature of this disease is the entire absence of that intense glial proliferation which characterizes all other chronic degenerative diseases of the spinal cord. The cord is not shrunken, as would be the case in sclerosis, but is a big, swollen, edematous cord. The lesion is essentially a degeneration with edema, and when you look at sections of the cord under the microscope, instead of seeing dense scar tissue in the diseased areas, it presents a honey-combed appearance where the nerve fibers of the white columns have undergone liquefaction. This appearance persists until death.

Of course, we have all been taught that regeneration does not take place in the cord; but, due to the pathological facts which I have stated above, i. e., absence of scar tissue formation and the persistence of the little holes in the white columns, it does not seem entirely impossible that, if the neuron from which the degenerated fiber springs is still alive and the pathological process can be checked by the use of liver extract, the axon might grow down into these little holes to its original distribution. As we know from our experience with anterior poliomyelitis, this regeneration takes a long time, so that observation over a number of years will be necessary to determine whether it actually takes place. Certainly we have not the right, according to my experience, to condemn these people to hopeless invalidism; but rather we can give them every assurance of marked improvement if the treatment is adhered to rigidly.

One point which should be stressed is illustrated by a patient with the flaccid type of ataxia. She had improved markedly on liver feeding, after four years of repeated relapses and transfusions. Her improvement had been so marked that she refused to take the liver or liver extract any longer, though she was cautioned about the possibility of the development of grave neurological symptoms. Eight months later she reported to the hospital, supported on one side by her chauffeur and on the other by a maid, utterly unable to walk without their assistance. Her hemoglobin at this time was 78 per cent and her red blood count was 4,800,000, but even though the blood picture had remained normal, the neurological lesion had progressed to an extreme degree. Her improvement on large doses of the extract was marked and rapid; and she is now able, after six weeks, to climb steps and go about wherever she pleases with the use of a cane. I think this case brings out strongly the fact that in spite of a complete remission in the blood condition, liver therapy should be continued without any break; don't let them stop at all, because these cord lesions, as one of the essayists has said, are the most serious aspect of the disease and should be guarded against rigidly.

DR. BEVERLEY R. TUCKER, Richmond: I should like to say, very briefly, that our experience has coincided in the cord cases with that of Dr. Williams. We treat a certain number of these cases but see many more in consultation than we actually treat. I think undoubtedly in the early stages and even in the medium stages the cord changes are purely toxic and absolute recovery may take place. They begin, as a rule, with numbness and tingling, and those cases can get well if treatment is persisted in. The surprising thing is not that they go into chronic invalidism but that under active and persistent treatment these cases may get well or may make a practical recovery. Of course, in long standing cases, where toxemia has existed for a length of time, degeneration has taken place; and I suppose nobody but God can replace degenerated nerve tissue. I think one of the best things the liver treatment has done is that it helps the prognosis in some of these cases. In the beginning cases and even medium cases, absolute recovery is possible.

DR. R. FINLEY GAYLE, Richmond: The cord changes following pernicious anemia have been mentioned by several, and for that reason I shall not attempt to discuss them here.

There is one central nervous change that has not been touched upon, and that is the cerebral changes accompanying not only the primary anemias but the secondary ones. We see some of these cases which have marked psychoses; some of them are of the manic depressive type, some of apparent intellectual deterioration, and some with emotional instability. Others have various degrees and types of aphasia. We now have one case under treatment who has a marked aphasia with a secondary anemia, and it is our opinion that the anemia has much to do with the aphasia.

DR. T. DEWEY DAVIS, Richmond: I am sorry that I missed the first two papers in this symposium, but I was very much interested in Dr. Flippin's paper on the medical treatment. Of course, the value of liver extract and of the feeding of whole liver has been thoroughly established, but there is considerable doubt in the minds of certain individuals as to whether this is the whole story in the treatment of pernicious anemia. Dr. Means, of Boston, in discussing the etiology, recently stated that he believes the lack of hydrochloric acid in the stomach probably has something to do with the development of the anemia, in this respect—that something happens or something does not happen in the digestion of the food as the result of the lack of hydrochloric acid, and this something plays a part in the development of the anemia. There are some men who believe that the giving of hydrochloric acid in pernicious anemia along with liver extract helps to prevent the cord changes and, not only that, helps to cure them after they have developed. I can recall three individuals with marked cord changes who were treated before the days of liver feeding. The principal part of their treatment was hydrochloric acid in doses of three to six drams a day, and all showed striking improvement in the cord symptoms. We cannot say positively that the liver extract has any specific effect on the cord changes, because we know the cord lesions will get well sometimes without the liver extract, and sometimes with the liver extract or whatever else you do there is no improvement in the cord changes. So I want to make a plea not to entirely disregard hydrochloric acid in the treatment of pernicious anemia. Not only does it in some cases aid the digestion, but I believe it is particularly of value in helping the cord symptoms.

DR. J. C. FLIPPIN, University, closing the discussion: In commenting upon the rather striking unanimity of experience and results of liver therapy in pernicious anemias, I did not mean to infer that our information in this field is by any means complete. This and other recent work on the anemias open a most interesting and fruitful field for further thought and investigation.

In the University Hospital in the past few months, we have been using a liver portion prepared under the supervision of Dr. Porter and his associates of the Medical College of Virginia. Thus far we have found this preparation entirely satisfactory in its therapeutic effects, and apparently quite as active as the Eli Lilly extract. As yet, I believe Dr. Porter and his co-workers have made no announcements with reference to their investigations, indicating a commendable attitude of conservatism on their part.

THE HIGH OBSTETRICAL DEATH RATE WITH SUGGESTIONS AS TO ITS CURE.*

By GREER BAUGHMAN, M. D., F. A. C. S., Richmond, Va.
Professor of Obstetrics, Medical College of Virginia.

Motherhood is one of the most important functions of woman. It should add to her happiness, broaden her usefulness and at least not interfere with her health.

We find unfortunately in the State of Virginia that deliveries are declining. There were 3,374 more women delivered in 1925 than 1926. Of this number the whites were lower by 2,262 and the colored by 1,112. In 1927 as compared with 1925 the difference was not so great but still significant. The total reduction, comparing 1927 with 1925, was 3,237, with a white reduction of 1,826 and a colored reduction of 1,401.

*Read before the fifty-ninth annual meeting of the Medical Society of Virginia, in Danville, Va., October 16-18, 1928.

XUM

With such figures before us, I think we are justified in stating that an increasing number of married women are refusing to become pregnant or if they do become pregnant are being interfered with. There were ten more white marriages in 1926 than in 1925 but 120 less colored marriages.

No one cause can be singled out as the true reason for the reduction in the birth rate. The main reasons might be found under the following (a) economic, (b) better jobs for women, (c) better education for women, (d) style, (e) a lessening of church and moral teaching, (f) fear of pain, (g) fear of morbidity, (h) fear of death, (i) spread of propaganda on birth control.

We will discuss briefly the three causes that seem to come within the province of the doctor.

I doubt that the fear of pain is a very deep seated cause. Those of my patients who discuss pain with me are the ones that have been dominated by a mother or grandmother, who were delivered before the doctors began to use the most painless methods of delivery.

The fear of morbidity and death are real. Are we doing all that we can to remove these two monsters from the path of the pregnant woman?

The study of morbidity is very complicated. It undoubtedly parallels the death rate so for the purposes of this paper we will discuss mortality.

The completed statistics for the United States as a whole are not available since 1926. During 1926, in the registration area of the United States the puerperal mortality rate reached the enormous number of 14,800—8,037 urban and 6,763 rural. During that same period Virginia with a population of 2,519,000 had 411 puerperal deaths, making 8 per thousand of births. This was thirty-three more than in 1925 in spite of the fact that there were 3,374 fewer babies born. Statistics show that 1926 had the highest obstetrical death rate since 1920.

Fortunately, the death rate declined in 1927. There were, in 1927, 364 puerperal deaths in Virginia, ninety-seven less than in 1926, with forty-seven more deliveries. This gives Virginia in 1927 a death rate of 6.3 per thousand compared with 8 per thousand in 1926, and the lowest death rate since 1912. The rate for sepsis was practically the same as it has been for many years but the rate for eclampsia was 1.7, being the lowest reported by 1 per thousand since 1912.

Either the State of Virginia or the committee for the study of the midwife problem in Virginia is lucky. This committee was appointed by your former President, Dr. J. Shelton Horsley, in the early part of 1927, to study the midwife problem. The committee enlarged its duties to include the study of deaths from the puerperal state and worked out a plan for reducing them. The State was lucky if what the committee did helped to reduce the puerperal mortality, while the committee was lucky, starting to work when it did, if the mortality was on the way down any how.

How may we cure the high puerperal mortality rate?

Fortunately, the greater number of puerperal deaths may be classified under two general heads—sepsis and eclampsia, as it is generally called, but more properly toxemia of pregnancy. If we can put these two great monsters that beset the path of pregnant women to rout, then we will be justified in claiming a great victory.

The death rate of the toxemias can be reduced to the vanishing point if we can prevent the toxic woman from having convulsions. We can prevent both toxemia and convulsions by prenatal care. This fact is as well known by the medical profession as that guarding the water supply and swatting flies will prevent typhoid.

If the public was as well informed about the prevention of toxemia of pregnancy as they are about the prevention of typhoid, then the mortality of the pregnant state would be greatly reduced.

Your committee has deemed it wise to indicate to the doctors of the state by letter, pamphlet, and by the reading of papers from time to time, that the line of attack against the high death rate from eclampsia is to stress prenatal care and to try to have all pregnant women see a doctor.

After the doctors of the state have learned of our plan we hope to tell the public the dangers of toxemia and sepsis too for that matter and to insist that the way to prevent them is to visit their family doctors at stated intervals for an examination, urinalysis, blood pressure reading and advice.

We have already instructed the county nurses to try to have the women who intend

to be delivered by midwives make at least one visit to the doctor of their choice or some nearby clinic for a similar examination.

We bespeak an interest and hearty co-operation on your part in this plan for the reduction of maternal mortality in the State of Virginia.

It is with pride that we point to the reduction of the eclamptic deaths by one whole point in 1,000 since we have been carrying on this propaganda. It is you and your co-operation that has reduced the eclamptic death rate. The committee is merely the noise that is scaring the women into your offices.

The reduction of the toxic death rate is comparatively easy. Any doctor who will devote time enough to his cases to make them come to him for examination, examine their urine, blood pressure and, in the event of trouble, outline a plan of diet and simple treatment coupled with the induction of premature labor when the case is not improving under the plans that he has mapped out, will reduce the number of cases of convulsions that he has in his own cases to two or three in his whole life time of practice.

The reduction of the sepsis death rate is a much more difficult problem. Your committee does not expect to make any sensational reduction in the sepsis incidence or death rate.

The mis-fit of the baby and pelvis, depending as it does upon the size of the baby, the size of the pelvis, the ability of the head to mould, tend to an early break of the bag of waters, necessitating frequent vaginal or rectal examinations to determine progress; and finally operative intervention is one of the most common predisposing causes of sepsis even in hospitals where examinations can be made under the most favorable conditions. Prolonged labor due to the above named cause coupled often with a rigid cervix due to old scar tissue is a very common cause of opportunity for infection. The lighting up of old infections, particularly gonorrhea, as a result of the mechanics of labor is a very common sight, particularly on the charity wards. Cross infections carried from one case to another by nurses or doctors are common. The traumatized cervix and perineum in even the most skillful hands is often the starting point of serious infection and death.

These and many other perfectly obvious predisposing causes of sepsis in hospital labors are a sufficient problem to handle. When we add to these the poor home surroundings, the even poorer care that the home delivery has, and any carelessness upon the part of the doctor in his examination, the problem grows to enormous proportions.

Prenatal care is in sepsis prevention an answer as well as in toxemia prevention. Unfortunately it gives only a partial answer.

A careful pelvimetry at the preliminary examination of the patient coupled with what is more important, a manual mapping out of the pelvis during the vaginal examination, will give a comparatively true picture of the probable outcome of labor. If to this primary examination is coupled a mapping out of the baby's progressive size by abdominal palpation, foetometry, and finally an X-ray examination, then we are in position to know what the outcome of the labor should be, and prepare for trouble.

A thorough knowledge of the case ahead of time almost precludes the necessity of vaginal examinations. I believe in vaginal examinations but they should be made many weeks before labor starts.

Unfortunately, the handling of a case as outlined is almost impossible for the busy general practitioner. It includes more training in accurate pelvimetry, vaginal mapping of pelvis, foetometry, etc., than we are able to give except in the most rudimentary way at the medical schools to the average medical student. Such a knowledge as he should have is predicated upon the careful examination and following of many hundred cases. Fortunately, the trend of the times in medical education is to give more hours to obstetrics.

Another part of the preventive work has to do with a clean delivery, a very clean delivery, a scrupulously clean delivery, a sterile delivery. This includes an absence of vaginal examinations at delivery and the reduction of rectal examinations to the minimum.

If in addition to the above we are able to practice and teach a God-like judgment as to the time, and to the method of interference, we would indeed drive sepsis out of our midst.

DISCUSSION.

DR. P. W. MILES, Danville: It seems to me that the obstetrical death rate in Virginia is entirely too high. Dr. Baughman did not tell us anything about the infantile deaths connected with it, for the large percentage of mothers losing their lives at that time means two lives, not only because of the death of the mother, but many of these children die in the first four to six days of life from lack of mother

care, I should say. The committee has worked hard to try to find some plan by which it could reduce this death rate. Better education of the laymen seems to be the greatest point that we could find for the present. I think the doctors are possibly doing everything it is possible for them to do, but they are practically almost helpless without the co-operation of the laymen. Strange as it might seem, there are many of these women in our cities and towns, and especially in industrial villages, that receive no prenatal care whatsoever. What we are going to do about it nobody knows, but it seems if we could educate the laymen even to the fear of death—that is, to the point where they know of the dangers of mortality and morbidity—we might accomplish something. How to bring about that education is hard to say. Possibly through the public health service, and by their publicity every pregnant woman will know something about the necessity of prenatal care and will go to some doctor for examination. I think this is a case where neighborhood gossip might be a virtue; women talking to each other will become impressed with the necessity of prenatal care and will go to a doctor to be examined.

DR. ROBERT P. KELLY, Lynchburg: I cannot add anything to what Dr. Baughman has said, but I do want to thank him for this excellent paper, which I think is one of the best I have ever heard on the subject. One thing he mentioned which I should like to emphasize is rectal examination. I feel that most of us can learn, with a little practice, to conduct these cases by rectal examination, making absolutely unnecessary vaginal examination, which is, of course, the worst thing we can do if we want to avoid infection. By rectal examination I think at least half of the sepsis cases could be prevented. My personal experience has been that most of the deaths I have seen, in the last five or six years, have been cases which have been badly handled in the second stage of labor. One or two of those deaths, when I saw the patient, were practically inevitable; the patients were almost dead when I saw them.

That leads me to another thing I want to emphasize, and that is calling for a consultation when in trouble or in doubt. I think there is not enough co-operation between the general practitioners and the men who pretend to specialize.

Another thing I should like to emphasize in the reduction of maternal mortality and infant mortality is the treatment of abortions. Of course, we all know that criminal abortions will frequently cause maternal mortality; but I think we often overlook the fact that spontaneous abortions will often result in infection and death, due to examinations, etc. As a rule, spontaneous abortion cases should not be examined within the first two or three months of pregnancy. Most of those cases will take care of themselves. I think the best way to treat such cases is to leave them alone for at least a week or more; then finally, if they do not clear up, I think it might be advisable to empty the uterus, but not curet them, not scrape them.

DR. PERCY HARRIS, Scottsville: I do not believe the imputation of the high mortality rate to the doctor is absolutely just. For instance, an obstetrician gets a high mortality rate because he gets the most complicated cases. Then the high mortality rate of the general practitioner is due to the incompetency of the midwife. If a woman has toxemia, a midwife knows nothing about albuminuria. It seems to me that in protection to the midwife as well as to the doctor, the midwife should be instructed, and when a midwife takes charge of a case the patient should be told to go to see a physician. If midwives are going to be licensed and turned loose on the public, they should first be properly taught. In the majority of cases of death of the mother, the doctor signs the death certificate, thus getting an increased mortality rate which he is not justly entitled to; because, as I say, the obstetrician will sign the death certificate in the most complicated cases referred to him by the general practitioner, and the doctor will sign the death certificate in the cases sent to him by the midwife. I should like to see the midwife educated so that she will call in a physician in any unusual or complicated case and do it before it is too late.

DR. BAUGHMAN, closing the discussion: I am going to say just one word. This paper of mine is not scientific; it is propaganda to help in the reduction of maternal and infant mortality. I promise you that your committee is going to do the best it can to reduce the death rate of mothers and infants. The committee is working absolutely along the doctor's lines, because we believe if you do not know a little more about how to prevent deaths you are right poor doctors, and we think you are right good doctors. We believe if we can get pregnant women to see you at least one time, particularly the ones the midwife will deliver, you can do something towards helping to lower the death rate; but if you do not see the case until she is nearly dead, then, of course, you can not. That is the theory on which we are going, and I hope we are going to have your heartiest co-operation. When you hear from us, perhaps over the radio, say to yourself: "Those fellows are trying to do the right thing to reduce the high mortality in obstetrics in the State of Virginia."

SOME OBSERVATIONS ON THE DYSPEPSIA ASSOCIATED WITH GALL-BLADDER DISEASE.*

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and
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While chronic cholecystitis and cholelithiasis frequently give rise to characteristic acute attacks pointing directly to the presence of these affections, there are many instances in which, due to atypical manifestations, the correct diagnosis becomes impossible. It not uncommonly happens that many of these cases present histories of dyspepsia of a rather chronic though mild type with an absence of the acute attacks of colic and jaundice without other direct evidence of gall-bladder involvement.

In an interesting publication Graham[1] has presented a detailed description of the chronic type of gall-bladder dyspepsia in which he urges the importance of obtaining in each instance a detailed history in addition to the usual clinical investigation in order to arrive

*Read at the meeting of the Baltimore City Medical Society, October 19, 1928.

at a correct conclusion. He points to the discomfort occurring soon after meals and radiating into the back, especially toward the right shoulder, and the history of acute attacks of indigestion as evidence of this type of gall-bladder disease. Blackford and Dwyer[2] have more recently called attention to this condition. They describe two clinical types of this disease.

(1) Attacks of gall-stone colic continuing for years and then the gradual onset of chronic dyspepsia; and (2) chronic dyspepsia with milder attacks of acute indigestion and often followed by biliary colic.

According to our experience the presence of gall-bladder dyspepsia may ordinarily be suspected if a thorough clinical history is obtained. Not infrequently the patient will be reminded of attacks of early acute abdominal pains some of which may have perhaps required anodynes for relief, and some may have been accompanied at times with jaundice or will present histories of early infections such as typhoid fever. Preceding or following such attacks, dyspepsia of a chronic though milder type has been noted with periods of relief extending over months or even years. The dyspeptic symptoms manifested are fullness, weight and distention following meals, though at times without relation to food, which may or may not be accompanied by discomfort in the epigastrium and under the right costal arch. These symptoms are frequently relieved by eructations or by means of carminatives. It is not uncommon for these paroxysms to occur just upon retiring, causing such distress as to require the patient to sit erect in bed for hours, producing forcible efforts at eructations. Pain is often noted following meals, extending around the upper abdomen, especially in the region of the right hypochondrium. It may occur in the form of the hunger type, reaching its greatest intensity three or four hours following meals, though this is not constant, and relief is ordinarily not always afforded by means of food or alkalies. Indigestible food is apt to aggravate this condition. Tenderness on pressure in the region of the gall-bladder is not uncommon though this sign is by no means constant. Nausea and vomiting occur at times. These symptoms are ordinarily not severe and may continue on for years, often with periods of relief following careful dieting or medical treatment, recurring at irregular intervals for shorter or longer periods, especially following indiscretions in diet or upon over-exertion.

While these forms of gall-bladder infections are ordinarily diagnosed without difficulty by the history of acute attacks as well as by the tenderness elicited under the right costal arch, notwithstanding the rather indefinite gastric symptomatology, other forms of cholecystitis occur in which the diagnosis is very uncertain and obscure.

In this group are the cases classified under the term biliousness. These patients are sallow in appearance, weak, affected with indigestion and constipation, and are the subjects of sick headaches and migraine attacks, with temporary slight enlargement of the liver. In many of such cases severe types of biliary stasis with chronic cholecystitis exist due to the presence of an atonic, infected gall-bladder.

In certain affections of the gall-bladder, notably in cholecystitis and cholelithiasis, pyloro-spasm is produced, resulting in epigastric pain with symptoms of hyperacidity. The condition may in consequence simulate gastric or duodenal ulcer or chronic appendicitis and, on this account, the diagnosis may thus be rendered extremely doubtful. Further, difficulty may also arise by the possibility of the two conditions being present in the same patient. In some cases dysphagia is a prominent symptom, due to reflex spasm at the cardia.

In another group of cases no history of severe attacks is presented, but only a grumbling gnawing sensation relieved by food and by alkalies with an associated hyperacidity.

In still a further type a septic temperature is observed of a greater or lesser severity with slight gastric disturbance or pain. The temperature may continue on with morning remissions and an evening rise for a considerable period of time until perhaps the true condition is revealed by a sudden onset of an acute attack of gall-bladder colic.

Finally, in another type which markedly simulates angina pectoris or coronary thrombosis, pain is noted in the precordium, radiating into the arm. There is often present in these cases considerable gaseous distention of the stomach with eructations not uncommonly of the aerophagic type. In consequence, such

patients are not infrequently treated for angina pectoris until an enlargement of the liver with tenderness under the right costal arch and, perhaps a mild increase in temperature will point out the true nature of the affection. In a considerable number of instances of this type, gall-bladder operation is followed by complete recovery. In many of the obscure cases of cholecystitis accompanied with gastric dyspepsia in which the diagnosis remains doubtful, the correct solution may be arrived at by means of X-ray examinations. The roentgen-ray indications of gall-bladder infections are revealed by the presence of adhesions dragging the stomach and duodenum over into the direction of the gall-bladder. The adhesions, however, need not necessarily extend from the stomach and duodenum, but may arise directly from the gall-bladder itself extending to various parts of the intestinal tract and are apt to produce varying degrees of stasis, retention and even obstruction according to their extent, and thus give us a definite picture in the plates as to the chronicity of the gall-bladder disturbance. Frequently this condition is associated with a filling defect in the duodenum and a deformity of the duodenal cap. When that condition arises, it is often extremely difficult to determine whether we are dealing with a primary gall-bladder or duodenal disease.

The demonstration of gall-stones by the roentgen-ray has proven of value in a certain percentage of cases depending largely upon the amount of calcium salts present in the stones. Gall-stones composed entirely of pure cholesterin are practically invisible to the ray on the plain plates, or when barium meals are employed. It is difficult to give percentages, as they vary so markedly according to the type of case and the operator that figures would be misleading. Visualization of gall-stones occurs, however, in probably less than 25 per cent of the cases. With improved technic, it is now possible to visualize the gall-bladder shadow even though gall-stones are absent, and it is ordinarily conceded that a gall-bladder that can be seen is diseased, i. e., containing either soft calculi, thickened bile or consisting of a hypertrophied wall. One must remember, however, that a negative diagnosis does not necessarily rule out gall-stones.

Finally, by means of the recent method of Graham and Cole[3], we have been enabled to visualize the gall-bladder. By injecting calcium tetrabromphenolphthalein intravenously these investigators were able to clearly visualize this organ in normal individuals. On account of the serious reactions which sometimes followed the intravenous injection of the dye, the oral method has been found more satisfactory, and an office routine similar to the opaque meal in gastro-intestinal investigations has been made possible. The technic we[4] have used has been briefly as follows: Five grains of sodium tetraiodophenolphthalein in enteric coated pills or capsules are given for every ten pounds of body weight. One-half of the total dose is given with a light supper at 6 P. M., and, beginning two hours later, the remainder of the pills are given, two every fifteen minutes untll all are consumed. The patient returns sixteen hours later for the X-ray examination. If stone shadows are found, or, if the gall-bladder is not visualized at this period, a positive diagnosis of gall-bladder disease is made. If the gall-bladder is filled, the patient is fluoroscoped for mobility and tender areas and requested to return one hour after eating a fatty meal.

Inasmuch as jaundice is observed only in a small proportion of instances following atypical gall-stone attacks, one cannot depend entirely upon this sign as an evidence of gall-bladder disease. However, since bilirubin is frequently increased in the blood following such attacks, the determination of latent jaundice in the blood by means of the Van den Bergh reaction or by the icterus index of Bernheim may be of considerable diagnostic help. The normal range, according to the Bernheim method, is between two and five and the index in clinical icterus is over fifteen. Latent jaundice is indicated by figures between six and fifteen.

As a further aid in the diagnosis of obscure forms of dyspepsia due to gall-bladder infections, the Lyon-Meltzer method of biliary drainage frequently presents considerable direct evidence. The diagnosis is developed, according to Lyon, around the direct study of the bile and the manner of its discharge, on the gross appearances of the specimens obtained, the quantity, color, consistency, viscosity, transparency, turbidity, flocculations, mucus, etc.; the cytological examination—epithelium, whether bile stained, its source, pus

cells, crystals, concretions, red blood corpuscles, inflammatory debris, mucus, bacteria; the chemistry—lecithin, cholesterin, calcium, pigments, effervescence on acidification, etc.; and by the bacteriology, as by culturation of samples of the bile. Failure to obtain gall-bladder bile after stimulation with magnesium sulphate indicates complete obstruction of the cystic duct, either due to stones, adhesions, or pressure from without by a tumor. Failure to obtain the clear lemon yellow bile or common duct bile is indicative of common duct obstruction. Of course, neither gall-bladder nor common duct bile is obtained when the common duct is obstructed. In these cases it is interesting to note that frequently by means of analysis of the duodenal contents, the pancreatic ferments are markedly diminished or absent. A mucoid discharge, bile tinged with flakes of red blood corpuscles, followed by a thin watery discharge, has been frequently observed by us in cases of partial obstruction of the common duct, while an excess of gall-bladder bile, that is over 90 c.c., is indicative of gall-bladder stasis. A diagnostic measure, which we have observed in a fair proportion of cases and which is of considerable value, is the pain produced immediately upon the introduction of the magnesium sulphate solution, which is much like a mild gall-bladder attack and is analogous to the pain occurring in cases of strictured ureters, or in Dietl's crises when fluids are instilled into the pelvis of the kidney. Inspissated mucus or tarry bile, extreme atony or atrophy of the gall-bladder, absence of bile in the gall-bladder, the contents consisting of calculi only, are other conditions in which the recovery of bile may be impossible even after stimulation.

In certain obscure forms of gall-bladder dyspepsia this method of non-surgical biliary drainage has, therefore, presented us with a valuable means of diagnosis. It is particularly valuable in that it enables us to diagnose these conditions early before evidence of complications have manifested themselves.

According to our experience achylia gastrica is present in from 20 to 25 per cent of these cases, while in from 25 to 30 per cent hyperacidity is observed. The association of achylia with pain or discomfort is rather indicative of organic disease, so that this finding may be of some value in diagnosis in certain obscure cases of gall-bladder dyspepsia.

In conclusion, it is evident that there are various types of gall-bladder dyspepsia in which the typical manifestations of this affection are absent and in which the diagnosis remains extremely obscure. In many of these instances a history of former acute attacks of upper abdominal pain may aid in arriving at correct conclusions. In some cases the diagnosis may, however, be cleared up by means of roentgen-ray examinations, while in others help may be obtained by means of duodenal drainage studies, the icterus index and the Van den Bergh reaction. There still exists, however, a small, but nevertheless, definite group of cases in which the diagnosis remains so obscure that only after prolonged clinical observation or even surgical intervention can a correct conclusion be reached.

The following brief histories present some of the unusual types of gall-bladder dyspepsia:

Case 1.—Case of cholelithiasis quiescent for a period of four years and then followed by symptoms of chronic dyspepsia.

A. T., male, aged 54 years, had had the usual diseases of childhood. At 22 he passed through a rather severe attack of typhoid fever which lasted about eight weeks. His convalescence presented nothing unusual and he remained in good health until about four years ago when he was suddenly attacked with severe pain in the upper right quadrant of the abdomen radiating to the back between the shoulder blades; accompanying this attack, chills, fever and sweats were noted and, on the following day, jaundice. This condition gradually subsided and after a week the patient had no further discomfort and appeared perfectly well. He continued in good health for four years, when indigestion of a rather severe type manifested itself. This consisted of fullness and distention and, occasionally, of pain following meals. These symptoms were often relieved by eructations and not infrequently recurred at night after retiring.

On physical examination, no abnormalities were detected with the exception of a slight tenderness noted occasionally under the right costal arch. An X-ray examination revealed distinct shadows of stones in the gall-bladder region. At operation a much enlarged gall-bladder, containing numerous stones, was found. The patient made an uneventful recov-

XUM

ery, and has since remained well and free from all dyspeptic symptoms.

Case 2.—Case of chronic dyspepsia, associated with attacks of acute indigestion, followed subsequently by typical attacks of biliary colic.

J. K., female, aged 39 years, had not been affected with any infectious disease with the exception of the usual ones observed in childhood, until at the age of 21 years, when she was the subject of a very severe attack of influenza, and passed through a prolonged course of chest involvement (broncho-pneumonia). At the age of 27 without evident cause she began to suffer with dyspepsia. There was present pressure and fullness following meals and occasionally pain, rarely nausea and vomiting. Attacks of indigestion would occur occasionally at night with pain in the epigastrium radiating toward the back, which were relieved by the frequent administration of soda in hot water. With the exception of a period of a month or two of relief at various times, the dyspepsia persisted for three years. Suddenly one night an acute attack of pain manifested itself, which radiated under the right costal arch into the back, and which required a hypodermic injection of morphia for relief. The attack was followed, after the second day, by jaundice which persisted for about a week. From now on the acute attacks increased in frequency so that operation was advised, at which time several stones were removed from the gall-bladder and common duct. This procedure afforded entire relief.

Case 3.—Patient affected with frequent bilious attacks; recovery following a course of non-surgical biliary drainages.

P. B., female, age 26 years, had frequent bilious attacks occurring at least twice each month in the form of sick headaches, nausea, vomiting of bile, followed frequently by a slight jaundice. These attacks persisted for from one to three days. Physical examination at this period revealed a definite enlargement of the liver with exquisite tenderness under the right costal arch. Non-surgical biliary drainages presented bile of a turbid type filled with mucus, pus cells and cholesterin crystals. Following a prolonged course of duodenal drainages, the symptoms gradually disappeared and the patient has now been relieved of all attacks for a period of several years.

Case 4.—Case simulating gastric ulcer, subsequently observed to be cholelithiasis.

P. F., male, aged 63 years, was affected with symptoms pointing to ulcer for years and had undergone numerous ulcer treatments with periods of apparent relief. The last attack was more severe, however, than all others and persisted for two months. The patient presented the usual signs of ulceration with attacks of pain appearing some time following meals, which were relieved by the ingestion of food as well as by alkalies. The gastric analysis revealed a hyperacidity, and the X-ray showed a large defect at the pylorus, which was interpreted as an ulcer with the possibility of beginning malignancy. At exploratory operation, the gall-bladder was observed much enlarged and filled with stones, and the defect noted in the X-ray plates was found to be produced by the pressure of the enlarged gall-bladder upon the stomach.

Case 5.—Patient presenting but little pain or other signs pointing to cholecystitis with the exception of a septic temperature.

J. C. McK., aged 46 years, had had the usual diseases of childhood, but otherwise enjoyed good health until four years ago. Without any obvious cause he began to show an evening rise of temperature, often as high as 101°, with morning remission to normal or below. This condition has continued ever since and, in addition, there has been a progressive loss in flesh, strength and energy, with indigestion in the form of acidity, eructations and flatulency.

On examination but few abnormalities could be detected with the exception of the evening rise in temperature. The thoracic organs were found to be normal and the abdomen soft; there was, however, a slight enlargement of the liver, and tenderness on pressure beneath the right costal arch. The blood pictures revealed a leucocystosis of 12,000 with 80 per cent of polymorphonuclear leucocytes. Biliary drainages revealed turbid specimens of bile filled with mucus and cholesterin crystals. Cholecystitis was suspected and operation advised. A much thickened gall-bladder containing dark inspissated bile, infected with colon bacilli, was removed. The evening rise of temperature soon disappeared and the patient has since remained well.

Case 6.—Case of cholelithiasis simulating angina pectoris.

Mrs. S. G., aged 35 years, was in good health until six months ago; since then there have

been attacks of precordial pain appearing mainly on exertion, though recently these have occurred at night, awakening the patient after sleeping quietly for several hours. These pains radiate down the left arm and are occasionally of sufficient severity to require opiates for relief. At times the pain has radiated to the abdomen. On physical examination the heart was found normal, and the blood pressure registered 140/80. The liver was slightly enlarged, and there was a distinct tenderness under the right costal arch. Several attacks were observed, which, though simulating those of angina pectoris, were of so mild a type as to give the impression that we were not dealing with true anginal attacks. During one attack the pain extended into the abdomen under the right costal arch, and around to the right shoulder blade. On the following day a slight icterus was observed. Operation was advised and a gall-bladder filled with numerous small mulberry stones was removed. The patient has had no further attacks.

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STERILITY IN WOMEN.*

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The subject of sterility is one of the most important and most interesting that engages the attention of the gynecologist. In the search for a cause of a sterile union there are a number of problems in both partners that must be considered. That at least 25 per cent of the sterile unions are due to the male is a fact apt to be overlooked. The majority of the women coming for sterility take it for granted that the cause lies with them, especially when the husband is a strong, healthy man.

It is not within the scope of this paper to deal with all the male defects that may cause sterility, but it is the duty of the gynecologist to determine the presence or absence of spermatozoa, their number, their vitality, and their morphology. This preliminary study is best made of a condom specimen, freshly obtained. Though there are instances of oligospermia, where conception easily takes place, it is a cause for relative sterility; with a less fertile female conception would probably not occur. Moench has made some interesting observations on the morphology of the human spermatozoa, and is of the opinion that male fertility bears a definite ratio to the percentage of normal sperm cells. This, also, has received a great deal of attention in veterinary practice, where it has been possible from a study of the sperm of bulls to determine their fertility.

Evans, in a study of fecundity in rats, has made some interesting observations. He has estimated, for different rats, their fertility index, and has found that when the indices of the male and female are multiplied and give a product of over sixty, the union would be followed by conception, and when less, the percentage fell off in a ratio that bore close resemblance to the diminishing values of the product. For example, male and female rats with an index of eighty each would bear offspring, while a male with an index of 100 and a female with thirty would have a sterile union.

There is good evidence to prove that exhaustion, physical, mental, and sexual, as well as the toxins of disease, and some poisons, lessen both the male and female fertility.

The examination for the male sperm is never to be omitted even with the history of other children by the male. I have had three instances of widowers with children who married a second time, and in each there was a complete absence of spermatozoa.

In 75 per cent of the cases, the cause lies with the woman, and the number of causes is almost legion. In a general way they may be grouped as:

1. Those that hinder the entrance of the sperm cells into the uterus and tube.

2. Those that hinder the entrance of the ovum into the tubes and uterus.

3. Those preventing the proper development and extrusion of a healthy ovum.

4. Those that make the uterus and tubes unsuitable for the nidation of the ovum.

5. Those obscure causes that may be termed bio-chemical.

First—Those preventing the entrance of the

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sperm cell into the uterus. Under this heading are to be classified those developmental or acquired conditions that cause an atresia of the vagina, or of the cervix. Most of the atresias of the vagina are acquired as the result of some inflammatory condition, most often diphtheritic. The congenital atresias are usually associated with some other developmental genital defects. Some authorities feel that perineal lacerations, vaginal prolapse, and shallow perineums that fail to hold the semen, account to some extent for sterility; also that retroversion, with the cervix pointing well forward, interferes with the proper entrance of the sperm cells. I feel that in cases where this is a possible factor, either the male or the female has a low fertility index. In retroversion, passive congestion of the uterus and the concomitant cervicitis are much more important factors.

Vaginal secretions, which are inimical to the sperm cell, at times inhibit the activity of the cells, or actually destroy them. As vaginitis is usually caused by an infection from the cervix, the lesions there are to be considered as the greater etiological factors.

The secretions from the cervix may inhibit the sperm cells in a purely mechanical way, by entangling them in mucus too thick to allow their migration to the uterus, or by a distinct inhibitive or destructive effect upon the cells themselves.

Some feel that the acute anteflexion may make the entrance of the sperm cells mechanically impossible. Against this theory is the fact that the uterus can pass blood cells which are considerably larger than spermatozoa.

Second—Those that prevent the entrance of the ovum into the tubes and uterus. In this connection, adhesions around the fimbria of the tube are the most frequent lesions found, and these are more often due to gonococcal disease than to infection caused by an extension from the cervix or uterus, or from the appendix. The tube itself is also likely to be involved, so that the simple freeing of adhesions does not always render the tube patent and capable of transmitting the ovum. The prognosis as to the relief of sterility is distinctly better in the ordinary coccal infections than in those due to the gonococcus. Tuberculosis of the tubes also prevents the ovum from passing to the uterus. Infantilism of the tubes, and adhesions around the ovary itself may likewise cause the same difficulty. It is possible that with retroversion, and consequent prolapse of the tubes and ovaries, angulation of the tube or the lack of proper approximation of the ovary and the fimbriae may be deterrent factors.

Third—Those preventing the proper development and extrusion of a healthy ovum. The most frequent cause of primary ovarian sterility is hypoplasia; with this are usually associated other evidences of genital infantilism. There may develop an acquired hypoplasia as the result of an infection, or it may follow radiation. This may be temporary or permanent, dependent upon the degree of the infection or the intensity of the radiation.

The capsule of the ovary, as the result of inflammation, may become so thickened that the Graafian follicle does not properly rupture.

Ovarian growths lessen the chance of conception, but they are by no means a complete hindrance. According to Graves, the endometriomata are usually associated with sterility, and the cystadenomata and dermoids, when bilateral.

In the amenorrheas associated with lactation, hypothyroidism, change of location and climate, and those connected with debilitating diseases, there is in most cases a failure of ovulation. Too frequent childbearing may cause a hypoplasia that may be permanent or temporary.

Fourth—Those rendering the uterus and tubes unsuitable for the nidation and growth of the ovum. In the primary causes of sterility the most frequent uterine condition under this heading is infantilism, which is associated with hypoplasia of the ovary. I am inclined to think that ovarian hypoplasia is oftener encountered than uterine infantilism. The uterine hypoplasia is usually of a low degree, and often disappears after a few years of married life, or treatment directed to stimulation of ovarian activity or uterine growth. Uterine polyps, uterine myomata, and hyperplasia of the endometrium lessen the chances of proper ovular growth. Some veterinarians claim that there is often an infection of the endometrium that produces ovular death or early abortion. Curtis claims that the endometrium is sterile except in ascending gonorrheal infections, and infections resulting from interference with pregnancy, and operative procedures on the

XUM

uterus. Retroversion is a relative cause of sterility; this is probably due to the passive congestion incident to the malposition.

Fifth—Obscure and miscellaneous causes. Consanguinity is a relative cause, as well as the later generations of a mixed race union, in which there is a distinct loss of fertility. There is some evidence that the absorption of spermatoxin from the semen may act as a preventive of conception; in fact, the injection into the female has been used experimentally to prevent conception. Various endocrine disorders have been credited a role in sterility, chief of these being the ovarian and thyroid.

There are instances of incompatibility in a man and a woman, both of whom have been able to procreate when mated with other individuals. This may be explained on the ground that both have a low fecundity index and, when each is mated to a partner of greater fertility, conception is possible. There is no satisfactory evidence to prove that individuals belonging to different blood groupings are less sterile.

While not always practical to follow a definite plan in the investigation of the causes of sterility, it is best to do so whenever possible. The following is the method which I have found of advantage. It is planned so that the simplest methods are the ones first employed, so that if at any stage a definite cause is found, the patient may be spared the rest of the examination.

a. General and sex life history.

b. Physical examination, both general and pelvic.

c. Examination of condom specimen of semen to determine number, motility, and morphology of sperm cells. If this proves satisfactory, examination of the vaginal and cervical secretions of the woman, post-coitus to determine the presence and life of the sperm cells. Should this prove satisfactory, and there are no gross pelvic anomalies,

d. the patency of the tubes is investigated after the Rubin method. In the failure of the gas to pass, and when there are no contraindications, the location of the obstruction is determined by radiography of the uterus and tubes after the injection of an X-ray opaque medium.

e. All of the above being normal, and failing to account for the sterility, a complete examination of both partners is essential. Principally the venereal infections that may have caused an epidydimitis or a prostatitis in the man or a cervical or tubal infection in the woman. This is especially important in the woman as a history of infection with her would help to explain the sterility and, if the infection be recent, a warning in regard to any instrumentation for tubal patency. In most of the cases that come for investigation, the sex act itself has shown no abnormalities; nevertheless, an investigation of this is in order.

Parotitis with ovarian involvement has often been given as a cause, but many authorities feel it is over-exaggerated. I have had only one patient with an ovarian involvement, and this doubtful. The matter of sterility has not come up with her for since that time she has used contraceptive measures.

Although the pelvic abnormalities are more often the cause of sterility than those connected with the general health, it must be remembered that at times tuberculosis, hyper- and hypo-thyroidism, the intoxication of syphilis, lead, and other poisons, may be factors. Diabetes may be associated not only with sterility, but also with loss of sex desire, and with the male, inability to copulate.

The semen is secured in a condom which should be tied and kept warm by placing it beneath the clothes, next the body, and delivered to the laboratory within as short a time as possible. In some specimens the sperm cells keep their vitality for hours, but it is well to impress upon the patient that the specimen should be examined, if possible, within the hour. The search should be for sperm cells, pus and bacteria. The number of sperm cells, their motility and their morphology is to be considered. Moench has done some nice work on the study of the morphology, and he has found that fertility bears a very definite relation to the proportion of normal and abnormal cells. Where the percentage of abnormal cells is high, fertility is low, and fetal deaths high. Some veterinarians (Williams and Savage), by plotting the percentage of normal and abnormal cells in bulls, have been able to predict the degree of fertility.

If the semen is satisfactory in the condom specimen, arrangements are made to examine the vaginal and cervical secretions after normal intercourse; if possible, within the hour. By this, one is able to determine the action

XUM

of the vaginal secretion, and that of the cervix upon the sperm cells. While the vaginal secretion is normally acid, it may be so excessively so that the sperm cells are hampered in their onward progress, or actually killed. With an aspirating syringe and a cannula, a specimen is obtained from high in the cervical canal. If cells are found that are normally active, it is to be inferred that they will make the grade to the uterine canal. This examination is not entirely free of error for the sperm cells may, at the time, have already passed the internal os, and those that were in the vagina been carried away. The cervical secretion may be inimical by mechanically preventing the entrance of the sperm; it may have a lytic or otherwise inhibitory effect because of its chemical nature (Kurzrock).

Carey was one of the first to attempt to determine the patency of the tubes and this he did by injecting saline solution through the uterus. Kennedy followed with the use of argyrol and radiography. The greatest impetus and the best single method is that of gas insufflation as elaborated by Rubin. At first oxygen was used, but the slow absorption from the peritoneal cavity made it less desirable than the carbon dioxide that is now used. In general, the method consists in inserting a cannula into the uterus beyond the internal os with a cone shaped rubber, of such shape and fitted on to it at such a distance from the tip, that it forms an air tight stopper at the external os. The gas is instilled at a pressure not to exceed 200 mm. of mercury, through an apparatus that measures the amount injected and shows the speed and the pressure of injection. At first Rubin radiographed these patients to determine the presence of gas within the abdomen, as it could be shown beneath the diaphragm within a few minutes after the patient had assumed the erect posture, if injected in amounts of 200 c.c. or more. This is no longer found necessary; if the apparatus is leakproof and there is no loss during the injection, one can assume that it has passed into the abdomen. By elevating the table and flooding the vagina above the level of the internal os with boric solution after the cannula has been inserted into the uterus, any escape of gas would make itself apparent by bubbling in the fluid. If one is successful in passing the gas into the abdomen, the patient experiences, on taking the erect posture, a most characteristic pain in one or both shoulders, due to phrenic irritation when the gas reaches the diaphragm.

Normally the gas passes through at a pressure of 40 to 80 mm., the initial pressure being the higher; this pressure may vary during the injection due to contractions of the tubes. A failure to get the gas through does not necessarily indicate closure of the tubes. It may be due to spasm, swelling of the mucosa at the uterine cornu, or to tubal angulations, as sometimes met with in retroversion. In marked hypoplasia of the tubes there may be failure due to small tubes, or the tortuosity seen in such cases.

The indications for the test are failure to find an apparent cause for the sterility in the tests that have been detailed before, and the absence of factors that make it dangerous. With a history of infection that may not have cleared up, with the finding of tubal masses after such a history, and a menstrual history that might indicate a possibility of a pregnancy, the test should not be done. The best time, according to the advice of Rubin is four to seven days after menstruation, and before intercourse has taken place. This obviates the possibility of interrupting an early pregnancy; it is also more favorable in that the uterine canal is more patulous, and there is less chance of forcing endometrium into the abdomen where it might be the starting point of an endometrioma, according to Sampson. Rubin also feels that if there is some slight obstruction it may be overcome, and that if coitus should take place soon after, at a time when a ripe ovum may be able to enter the tube, the chances of pregnancy are greater.

Failure of the passage of the gas indicates the probable closure of the tubes but the site of the obstruction is still in doubt; although pain in the sides of the pelvis might lead one to suppose that the blockage was at the distal ends of the tube, and that the pain was due to tubal distention.

Passage of the gas at high pressure indicates a probable hindrance due to spasm, adhesions, kinking, etc., especially if after an initial high point the gas begins to flow at a lower pressure.

If there is a failure of the gas to pass or it passes at high pressure, the test should be repeated at another time, after a hypodermic

injection of 1/100 grain of atropine to overcome any spasm.

As the Rubin test does not give an idea of the point of tubal obstruction, in the cases that are negative to his method, the next procedure is to radiograph the tubes after the injection of lipiodol, which is a mixture of iodine in oil. A cheaper preparation, and one equally good, is iodopin (Merck). This is done by placing the patient in the lithotomy position on the X-ray table, inserting a bi-valve speculum, grasping the cervix with a tenaculum, inserting into the uterus a cannula similar to that used in the Rubin test and injecting the warmed lipiodol into the uterus. A radiograph is then made while the pressure of the syringe used for the injection is continued. Should the tubes be open and a moderate amount of the oil be injected into the peritoneal cavity, there is no harm done. If there is doubt as to whether oil has been injected into the peritoneum, the patient is radiographed the next day, when the injected oil will be found in the cul-de-sac. However, this method is reserved for the cases in which tubal obstruction has been proven by the Rubin test. In this way one is able to determine the point of obstruction in the tube or tubes, and whether or not a relief operation should be attempted.

In the absence of causes of male sterility the greatest number of the cases seen are those due to hypoplasia of the uterus and ovaries, cervical infections, and tubal obstruction, the first and the last being the most common. Of course there may be present more than one causative factor.

In the hypoplasias, if of slight degree, there is a chance that the stimulus of married life may, after a time, overcome this. In spite of the opinion of other authorities to the contrary, I believe that some of the patients have been benefited and have conceived as a result of the administration of gland products; my experience has been almost entirely with lutein. Dilatation of the uterus, either done in the office with sounds, or the more forcible dilatation under anesthesia, with and without stem pessary, has given some good results. Where there is oligomenorrhea, amenorrhea, Rongy, Rubin, and some others have noticed an improvement in the amenorrhea and a relief of the sterility by small doses of X-ray. The good effect has been explained, quoting from Graves, by the direct stimulation of the ovarian functional cells, the destruction of a persistent corpus lutein (Thaler), that has been inhibiting ovulation and menstruation. Geller feels that there may be inferior follicles that interfere with the normal maturation of others and that the destruction of these inferior cells releases the block. Rubin reports the cure of nine out of twelve cases in which there was an associated amenorrhea, and Rongy has had success in eight out of thirty-six cases of ovarian sterility. The dosage in the amenorrhea has been 10 to 15 per cent of the skin erythema dose, and with those with oligomenorrhea 5 to 10 per cent. While it is a well known fact that X-ray, both in humans and animals, may cause deformities of the fetus, in none of the cases mentioned has there been any deleterious effect on the offspring.

Several years ago, I had a talk with my friend, Dr. Robert T. Morris, on sterility in women who showed stigmata of degeneration with hypoplastic genitals, and he brought up the question as to whether it were wise to attempt to help these women overcome their sterility, as he felt it was a provision on the part of nature to curtail the reproduction of individuals who might be more unfit than their parents. The children I have seen born of women in whom the sterility has been overcome, seem to be as fit as others. It would be interesting to follow the history of their progeny and determine if there was a lack of fertility in them.

Cervical infections and lacerations should be looked after by appropriate operations, cauterizations and local treatments. Personally, I do not believe that these conditions have much bearing on the subject.

Retroversion, I feel sure, is a relative cause of sterility, and I have seen a number of conceptions take place after operative or pessary correction.

Tubal obstruction is one of the great causes, and in secondary sterility, I believe leads all the rest. If it is the result of an infection following labor or abortion, operation on the genitals, or appendicitis, the chances of overcoming the occlusion are better than when the condition is due to gonorrhea. Where the tubal obstruction is near the fimbria, the hope of relief is better than when it involves the whole tube or the uterine end.

Some of these obstructions are overcome by

the gas insufflation. Indeed, this experience has been so general that we now regard the Rubin test as not only a diagnostic but a therapeutic aid. Moench, in analyzing the cases in my clinic, found that conception took place in 8 per cent. In my private practice, I am sure the percentage is higher than this. I have three patients in whom the primary sterility ceased after the first inflation, and subsequent pregnancies have followed insufflations after a relatively long, secondary sterility.

One should be cautious in offering any hope in the relief of tubal sterility, especially if the obstruction is at the isthmal portion of the tube. Where there are only fine adhesions around the fimbria there is hope of conception after the freeing of them. In some instances, success has followed salpingostomy. Implantation of the tube into the uterus after the removal of the obstructing cause in the proximal portion has rarely succeeded. Morris and Estes have reported pregnancies after the implantation of a portion of an ovary into the cornu of the uterus. In Morris's case the ovary was obtained from another woman; this brought up the question as to who was actually the mother of the child.

Conclusions: Modern methods have made the study of sterility most interesting, and at the same time have laid a heavier duty upon the gynecologist.

By these methods he is able, in most instances, to determine the cause of the condition and, with this knowledge, he is able to plan a successful treatment. Likewise, such examinations may show the futility of any measures and the patient is spared needless operations.

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SURGICAL TREATMENT OF HEAD INJURIES.*

By J. COLEMAN MOTLEY, M. D., F. A. C. S., Abingdon, Va.

There was a time when head injuries were regarded as a major surgical problem only in the fairly large industrial centers. Since, however, improved roads have become universal and the whole country has become motorized, the automobile has won a place as one of the captains of the battalion of death; and injuries of the head are a matter of interest and concern to every road-side doctor. This is regarded, therefore, as a very timely subject; and the Executive Committee is to be congratulated on choosing it for discussion at this meeting.

When one is confronted with the care of a head injury, the most important consideration is: What has happened in the intracranial cavity. Except as it produces brain trauma, or acts as a barrier to the treatment of such a lesion, fracture of the skull, *per se*, may be largely disregarded. According to Sachs, one of six things may happen in a severe head injury:

A. Compound fracture with or without rupture of the dura.

B. Simple depressed fracture.

C. Intracranial hemorrhage.

D. Contusion and laceration of the brain.

E. Edema of the brain.

F. Rupture of the arachnoid with the escape of cerebro-spinal fluid into the subdural space.

To take up the indications for treatment in the same order:

Compound fracture of the skull would be dealt with according to the same surgical principles as would apply to lacerated wounds elsewhere. After thorough sterilization, a complete debridement would be made of all lacerated, devitalized and grossly soiled tissue. Soiled bone fragments should be removed. If bone fragments are reasonably clean and attached to dura, they may be saved. Owing to the fact that the skull is not a weight-bearing structure, fragments of bone may be sacrificed more generously than in the case of fracture of the long bones. In caring for compound fractures of the skull, wound soiling and infection constitute one of our major problems. If the dura is torn, it should be sutured, if possible. If the patient is seen early and gross soiling is not apparent, the wound may be completely closed. Usually, however, it is wise to use temporary, subdural drainage. Late cranioplasty to cover defects is sometimes required.

Basal fractures, while they are in fact compound, present quite different problems, because of the fact that the avenues of infection are more or less inaccessible to surgical approach. They communicate with the surface by way of the nose, throat or ear, depending on the cranial fossa involved. While it is true that basal fractures have been operated

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upon by brain specialists with good results, it is my personal conviction that, in the hands of the average general surgeon, these cases had best be treated by the more conservative procedures of brain shrinkage and spinal puncture. When operation is performed, it consists of a subtemporal decompression.

Fractures involving the paranasal sinuses are particularly fatal. If it is impracticable to operate on such a case immediately, then one had best postpone surgery for a week or ten days, or more, thus giving time for the avenues of meningeal infection to be sealed over by adhesions. Early drainage is important. If cerebro-spinal fluid is escaping from the nose, an attempt should be made to close the laceration in the dura.

All simple depressed fractures should be operated upon as soon as practicable after primary shock has been overcome. Systolic blood pressure of 60 or less and subnormal temperature are regarded by us as evidence of a degree of shock contraindicating surgery. When the depressed pieces of bone are elevated, large fragments may be removed and kept in warm saline solution. After the dura has been inspected, lacerations repaired and hemorrhage controlled, the fragments may be replaced in the defect and the scalp flap closed. In case of blood clot, or considerable collection of cerebro-spinal fluid beneath the injury, it is best to provide for temporary drainage. Fracture of the inner table of the skull requires the same treatment. Depressed fracture of the newborn, resulting from birth trauma, sometimes requires decompression.

A progressive rise in blood pressure following head injury indicates intracranial hemorrhage. Localized intracranial hemorrhage is a positive indication for prompt operation.

While a detailed discussion of cerebral localization lies outside the limits of this paper, it is nevertheless a fact that localization is, perhaps, the most important problem in the surgery of intracranial hemorrhage. The hemorrhage is not always at the point of skull fracture. At times there is severe hemorrhage without fracture. If there are constitutional symptoms pointing definitely to intracanial hemorrhage, upon which side of the skull shall we operate? Extradural hemorrhage of arterial origin is usually due to rupture of the middle meningeal artery, or its anterior or posterior branch. This is a rather fortuitous circumstance, for the hematoma is thus located in the temperoparietal area and produces sufficient pressure on the motor cortex to cause definite focal symptoms.

When, however, the hemorrhage has occurred in a silent area of the brain, its accurate localization requires considerable diagnostic skill, and the problem may tax one's resources to the fullest. In such a case, the cooperation of an oculist and an internist, trained in neurological observation, are extremely helpful. It is almost trite to state that intelligent treatment of head injuries without the aid of the X-ray is practically impossible.

Rutherford, Greenleaf and others have made the interesting observation that unilateral intracranial hemorrhage produces a difference in temperature on the two sides of the body. A higher temperature in one axilla than in the other indicates cortical irritation from hemorrhage on the opposite side.

Venous extradural hemorrhage is most frequently due to the laceration of a venous sinus. Sometimes it results from injury to a paranasal sinus. Intradural hemorrhage is due to the rupture of a venous sinus or the veins of the pia-arachnoid. Diagnosis is extremely difficult. Subdural hemorrhage occurs between the dura and the arachnoid. This condition is probably more common than extradural hemorrhage. Such a hemorrhage may be localized or diffuse; and bleeding may occur from sinuses or superficial vessels. Diffuse hemorrhage is usually the result of injury to a venous sinus.

It is desirable not to ligate a sinus if this can be avoided. Sometimes a small rent in the sinus wall can be closed by a purse string suture of silk, or the edges of a lateral tear can be sutured together. When one of these maneuvers is impossible, the sinus must be doubly ligated.

If one has to operate for fissure fracture with evidence of intracranial hemorrhage not accurately localized, it is best to make the trephine opening where the fracture line crosses the chief vessel of that region. The object of an operation for intracranial hemorrhage is to ligate the bleeding vessel, remove the blood clot, and repair the lacerated dura. Subtemporal decompression often fails to accomplish this purpose.

Intracranial hemorrhage of the newborn is

due to birth trauma. Such cases have sometimes been operated upon. My own experience in the treatment of this condition has been limited to spinal and ventricular puncture. I believe this to be the therapy of choice.

Contusion, or Laceration, and Edema of the Brain: As these conditions are usually associated, the one with the other, and as the symptoms are due to the combined effect of the two, consideration of their treatment will be taken together.

No tissue becomes edematous as rapidly as the brain. The symptoms of brain edema are those of increased intracranial pressure. The indications for treatment are:

1. The various brain shrinking methods, such as magnesium sulphate by mouth or per rectum, hypertonic solutions of magnesium sulphate, sodium chloride or glucose, intravenously. The results of this method of treatment are particularly gratifying in cases of brain laceration and diffuse edema.

2. Ventricular puncture and spinal puncture to remove fluid from the cavity and give the brain more room. Spinal puncture is particularly useful as a diagnostic measure, and the spinal fluid pressure is a fairly accurate index of the intracranial pressure. This procedure is, however, not without danger; and, if repeated spinal puncture is resorted to as a therapeutic measure, the fluid should be released slowly and guardedly.

3. The more conservative methods having failed, subtemporal decompression should be considered. If the pulse pressure continues to rise until it equals the pulse rate, it is an indication of extremely dangerous intracranial pressure.

The symptoms of ruptured arachnoid are not unlike those of middle meningeal hemorrhage, except that there is no increase in blood pressure. The surgical treatment of the condition involves a craniotomy. On nicking the dura and allowing the yellow, or blood stained fluid to escape, there is rapid improvement in the symptoms. The so-called free interval between the head injury and the beginning of symptoms may be hours, weeks, months, and even as long as ten years.

The extremely delayed onset of symptoms is due often to traumatic aneurisms of the cerebral vessels, which finally rupture. Of the late results of head injury, epilepsy is the most common. This is usually of the Jacksonian type, developing on the side opposite the injury. Cranioplasty should be advised where there is definite evidence of pressure on the cerebral cortex; but the results of surgery are not particularly encouraging. Sometimes the condition is aggravated by operation.

To summarize: In the treatment of head injuries, the fractured skull is of minor importance. The various conservative methods of treatment, such as brain shrinking, spinal and ventricular puncture, have, in my experience, contracted the field of emergency cranial surgery to cases of compound fracture, depressed fracture, intracranial hemorrhage, and intracranial pressure not relieved by non-surgical treatment.

As a rule, I do not operate on a brain injury unless definite localization can be made. The surgical objective is to expose and repair the lacerated dura, remove compressing substances and control hemorrhage. Routine subtemporal decompression fails because it does not remove the compressing substance nor control the hemorrhage. No case of head injury associated with even transitory unconsciousness should be regarded with professional indifference.

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HEAD INJURIES—NEUROLOGICAL SEQUELAE.*

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In discussing the neurological sequelae of head injuries, we shall leave out of consideration the immediate nervous and mental symptoms because they are really symptoms and not sequelae; sequelae are lesions or affections following or caused by an attack of disease or an injury. In head injuries, we may have all degrees of trauma, various methods by which the force is applied, various locations and positions to and in which it may be applied, and an important fact to be remembered is that the brain is an encapsulated or-

*Read as part of a symposium on Head Injuries before the Southwestern Virginia Medical Society, at Wytheville, Va., September 27-28, 1928.

gan and that the skull, or capsule, is absolutely inextensible by any physiological force. Therefore, any swelling of the brain or the intrusion of a foreign substance into the cranial cavity must cause a corresponding displacement of some material or other from within the skull. Damage resulting thereby interferes with the normal functioning of the most important portion of the central nervous system. When we consider the relative frequency with which the brain is subject to varying degrees of trauma ranging from slight concussion and contusion, squeezing during difficult labor, pressure from temporary deformation of the skull, fractures and penetrating wounds, the real wonder is that we do not see a much larger percentage of serious neurological sequelae. Refined diagnostic methods with suitable early surgical intervention in hemorrhage and depressed fracture cases probably help to keep low the percentage of unfavorable after-effects.

Without attempting to differentiate as between the various degrees of trauma and the different methods by which the force is applied, and the different types of injury resulting from the one or the other, we shall simply enumerate in the order of their importance the various neurological sequelae and discuss each from several standpoints.

I. *Epilepsy:* Recurring convulsive seizures are occasionally the result of a known head injury. In some cases epilepsy may occur years after the injury from a scar, a degenerative process of the cortex or a small cyst, any of which can result as a late complication of skull fracture. Yet, epilepsy is infrequently actually the result of trauma. We know that the alcoholic, the luetic, the neurotic and the degenerate are the progenitors of the epileptic. In some cases epilepsy can be traced to injuries of the head at birth. These are, however, usually the distinctly focal ones, or the Jacksonian type. The focal epilepsies are often amenable to surgery. True epilepsy, whether congenital or traumatic, usually is not. Surgery, however, is most valuable as a preventive and the early rational treatment of depressed fractures, or compression from clot or serum, lessens the chances of the patient for a neurological or psychiatrical complication. Many so-called cases of traumatic epilepsy following concussion are actually cases in which the soil was fertile and the trauma only the exciting factor. There is no particular type of head injury especially liable to produce it and patients who have Jacksonian fits as an immediate symptom seem to have no peculiar liability to become epileptic later. The treatment of a given case of epilepsy, resulting from trauma, and which is not amenable to surgery, is no different from the treatment of epilepsy in general. The routine administration of luminal following head injuries is valuable in preventing subsequent convulsive seizures.

II. *Mental Deterioration:* This occurs in varying degrees and, as in epilepsy, the serious cases are usually predisposed and the trauma the exciting factor. As a result of intracranial hemorrhage at birth we may have mental deficiency ranging from a low-grade imbecile to a backward child. After concussion, the recovery from which is usually complete and permanent, we may have appear, weeks or months after the injury, an entire change in the nature of the patient, manifested by egotism, selfishness, irritability, outbursts of violent rage about trivials, and forgetfulness. This forgetfulness is particular as to recent events. There are at times long gaps of memory. Less rarely actual insanity may arise, usually from the injuries causing brain destruction.

III. *Headaches:* Headaches following head injuries are usually the result of unresolved contusions with consequential cerebral irritation. They are often persistent and intense; occasionally they disappear spontaneously. Usually they are not localized. Often they are accompanied by insomnia, depression, and lassitude. In severe cases, there are sometimes mental symptoms. Usually the slightest exertion precipitates an attack, and it may last for several hours to several days. As long as the patient remains quiet and lives a life of ease, he is fairly comfortable; but any occupation necessitating physical exertion brings on attacks, and he sooner or later finds himself utterly incapacitated from performing any labor. In many of these cases, a sub-temporal decompression brings about immediate relief. Free saline catharsis is especially valuable.

IV. *Vertigo:* Dizziness or dizzy spells may follow any type of head injury but most commonly are the result of concussion. Unlike

post-traumatic headaches, there is very little hope for relief, surgically or otherwise. Outwardly, the sufferer is well and physical examination is usually negative, but on slight exertion, exposure to the sun, or to stimulants, he becomes dizzy. This dizziness may be manifested in all degrees and may last from a few minutes to days.

V. *Spastic Paralyses:* The spastic types of paralyses are unimportant because they are relatively rare. They may be present in the form of either monoplegia, diplegia, or quadriplegia. Usually they are accompanied by focal epilepsies. Surgery is helpful in most of these cases.

VI. *Cerebral Palsies:* Palsies of cerebral origin are usually the late results of head injuries at birth. They are rare.

VII. *Post-Traumatic Neuroses:* Following blows on the head, we may have every type of neurosis. Usually they are temporary. In cases where they are permanent, the trauma is usually only a contributing factor. After concussion the susceptibility to alcohol and to sunlight is markedly increased, and quick fatigue is characteristic.

ADAMANTINE EPITHELIOMA—REPORT OF A CASE.*

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M. R., age 60 years, female, admitted to St. Philips Hospital on November 25, 1927, was referred by Dr. J. R. Grinels.

Chief Complaint: Large tumor of chin, extending to both sides of the lower jaw; difficulty in mastication of food and very little pain.

Family History: Negative.

Past History: Patient has had the usual childhood diseases; influenza in 1918; slight rheumatism in the knees several years ago. No serious illness. No operations nor injuries. The cardio-vascular, respiratory, gastro-intestinal, and genito-urinary systems are negative. The menstrual history was normal with menopause at the age of fifty.

Present Illness: The patient dates the onset of her trouble to twelve years ago, with the extraction of two lower teeth in the right molar region which she thought were abscessed. Since then there had been intermittent enlargement of the lower jaw on the right side about the chin. The patient spoke about abscesses rupturing and draining inside her mouth. There was no history of pain or fever. After the rupture, the drainage would cease, and the swelling reappear. Since January, 1927, the swelling has been progressive, enlarging the chin and extending to both sides. The swelling has been greater on the right, causing the tongue to be pushed up and to the left. There has been no ulceration nor bleeding, and very little pain. The patient has lost some weight during the past year, presumably due to the inability of mastication and insufficient nourishment. There have been no tumors elsewhere in the body.

Physical Examination: The patient is a well developed and fairly well nourished female beyond middle life. The skin and mucous membranes are clear. There is no general glandular enlargement.

Fig. 1.—Appearance of patient before operation, showing enlargement and protrusion of the chin. The lower front teeth are widely separated and displaced forward and above the upper.

Head and Neck: The patient shows a large swelling of the lower jaw involving the chin and lateral aspects on either side to the molar region. The swelling is smooth and even in outline and is about the size of a large orange. The lower lip is forced forward and upward by the mass. Inside the mouth the swelling involves the alveolus. The lower front teeth are present but forced out of their normal position in a forward and upward direction and appear as widely separated pegs in the tumor.

*Read before the Richmond Academy of Medicine, February 28, 1928.

These teeth are loose. The tongue is pushed upward and to the left by extension backward of a soft tissue mass in the floor of the mouth on the right side. On palpation the tumor of the chin is firm and hard as bone in places, and in others the wall yields somewhat on deep pressure with a parchment like crepitation. There is no special tenderness about the tumor. There is no ulceration nor bleeding surface. There is no glandular enlargement in the neck.

The pupillary reactions are somewhat sluggish.

The neurological examination is negative.

Heart and lungs are normal.

Abdomen: Normal.

Extremities and reflexes are normal.

Laboratory Examinations: The urinalysis was negative for albumin, sugar, casts, pus, etc.

Hemoglobin 80 per cent. Red cell count: 3,816,000. Leucocytes 8,400. Polys. 58 per cent; small lympho. 30 per cent; large 8 per cent; and large monos. 4 per cent.

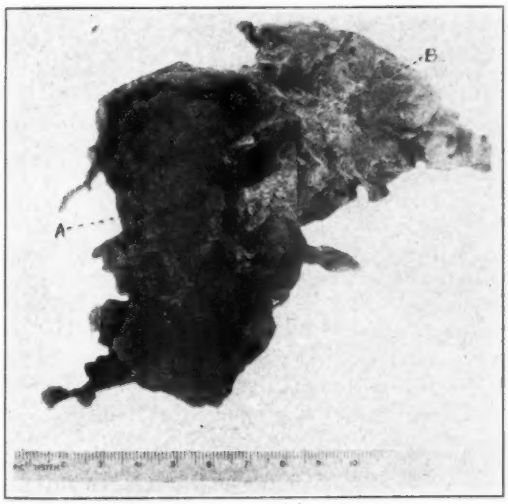

Fig. 2.—Gross appearance of tumor after removal.
A. Cystic portion removed from the chin.
B. Solid portion located in the floor of the mouth on the right side.

The blood Wassermann was negative.

The roentgenogram reported by Dr. J. L. Tabb was as follows:

"Much bone destruction is noted on the anterior aspect of the mandible which extends backward on the right side to the molar region, and backward on the left side to the molar region. The cortex of the bone has such marked expansion that it is hardly visible. The condition is probably a very extensive cyst of the jaw."

Diagnosis: Adamantinoma, or probably a dentigerous cyst. Malignancy of the tumor was considered. It was not likely, due to the duration of the growth of twelve years, absence of ulceration and glandular enlargement and the cystic appearance of the growth.

Operative removal was advised.

Operation: On December 2, 1927, under local anesthesia, later enhanced by ether, the operation was started, first, by extraction of all the lower front teeth involved in the tumor by Dr. A. M. Wash. An incision was made beneath the lower border of the mandible from near one angle to the other. The skin and soft tissues were easily separated from the wall of the tumor as far as it was necessary to give adequate exposure. The wall was ruptured through a soft area and a pocket of the cyst evacuated of a straw colored fluid. On further exploration of the inside of the tumor it was found to be multilocular, with the cysts varying in size and separated from each other by partly fibrous and bony partitions. The fluid of the different pockets varied from a thin straw color in some to a thick tarry appearance in others. The pressure of the cyst had caused a marked thinning and absorption of the mandible so that there was only a very thin shell of bone in places. The lower posterior portion of the wall of the tumor was composed of thicker bone, and it was thought advisable to preserve this portion of the mandible to give support after the tumor was removed. The thin membranous lining of the cysts was easily separated and removed from the surrounding bone and soft tissue. Extending backward in the floor of the mouth on the right side was a soft tumor mass about 5 cm. in diameter. This was removed chiefly by blunt dissection. It appeared to be encapsulated. The lining membrane of the cyst and the solid tumor appeared to be entirely removed. The posterior bony wall was preserved to support the jaw. The wound was closed with drainage. The patient entered the operating room with a pulse of 118 and left with 130.

Post-Operative Course: The patient reacted normally from the anesthetic. The wound healed by primary union and without

infection. The temperature ranged around 100, on several occasions 101 F., for one week, and then became normal. On the second post-operative day the urinalysis was negative, and on the fourth the leucocyte count was 9,600. On the tenth day she was up and walking about in the room, and the wound was completely healed. The cosmetic result was good. She was discharged on the sixteenth post-operative day. A recent communication from her family doctor stated that the patient has been in good health and that there had been no signs of recurrence of the growth.

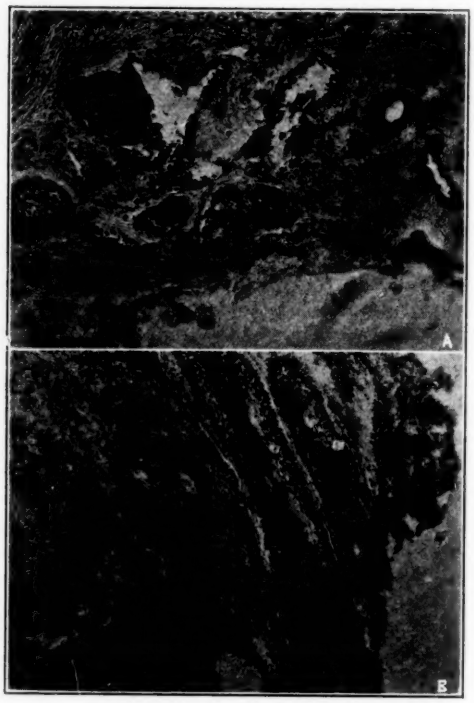

Fig. 3.—Photomicrograph of tumor under low power study.
A. Whorl-like nests of epithelial cells are seen, also cystic areas surrounded by epithelial cells. The stroma here is mostly fibrous and not very cellular.
B. Columns of epithelial cells the outer layer of which is of the cylindrical type. Many cystic areas are seen. The stroma here is very cellular. H. & E. Stain.

Pathological Report

Dr. Chas. H. Phillips presented the following report:

"Gross Description: The tumor mass is a bony shell about 5 cm. in diameter, bordered on one side by a hemorrhagic membranous tissue about 10 cm. long and on the other by a pinkish-white lobulated mass about 5 cm. in diameter. The surface of the mass is partly covered by a mucous membrane, suggesting the gums, and partly by cauliflower-like gray, flattened projections.

"Microscopic Description: The tissue shows a diffuse growth of modified squamous epithelium, often arranged atypically and in places undifferentiated. Much of this hyperplastic epithelium suggests origin from the buccal mucosa, and in places there are found poorly developed epithelial whorls. Some of the epithelium is of the transitional type. There are several small cystic cavities partially lined with a sort of a cuboidal epithelium and some small groups of the same cells appearing as if about to become cystic. There is also present some chronic inflammatory reaction and some necrosis in places. It is difficult to assign definite origin to this epithelial process but the transitional type of cell and its apparent tendency to line cystic spaces could fit in with an adamantine carcinoma. The process does not appear to be highly malignant now, although the degree of hyperplasia is notable and suspicious.

"Pathological Diagnosis: Cystic adamantinoma of the mandible."

Discussion: Adamantin epithelioma is known by many names, such as adamantinoma, adamantinoma cysticum, multilocular cyst, and adenocarcinoma. It is one of the classes of odontomata described by Bland Sutton. According to Malassez, it arises from the epithelial debris about the enamel organ in the development of a tooth. The duration of the growth is over a number of years, as much as twenty to thirty years having been reported. It is a benign tumor, but it must be borne in mind that malignancy sometimes takes place especially on recurrence after removal.

The tumor has a fibrous tissue stroma which may vary considerably in the amount of fibrillary and cellular material. In the present case the cellular content of the stroma was abundant in places. In this fibrous stroma occur nests or columns of epithelial cells. The cells of the outer layer are columnar or cylindrical, which is a characteristic feature of this type of tumor. The epithelial cells frequently resemble the stellate cells forming enamel. The center of this nest of epithelial cells may show degeneration, which undergoes liquefaction, resulting in a small cyst. There are many cysts throughout the tumor which vary in size due to the fact that several cysts may fuse with

one another by degeneration of the intervening tissue separating them. The growth and pressure of the cyst inside the mandible cause a thinning of the bone. Usually the anterior wall of the mandible is more destroyed than the posterior. This was true in the case here reported.

Fig. 4.—Photograph of patient 15 days after operation. Notice the normal facial features, contour of the chin, and inconspicuous scar.

From the surgical standpoint, after complete primary removal, the tumor does not recur. It is not necessary to resect the lower jaw to effect a cure, but it is very important to remove all the lining membrane of the cysts and solid tumor tissue. The thicker portion of the bony wall, usually the posterior, should be preserved to support the mandible and prevent deformity as far as possible.

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ADVANCES IN DIABETIC THERAPY SINCE THE USE OF INSULIN.*

By
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Due to the research and work of Banting, Best, Joslin, Allen and a host of others, the world has been made safe for the diabetic should he choose to learn and live. Recently before the New York Academy of Medicine, Joslin made the statement that the non-diabetic is fortunate to be able to live as long as the diabetic, the age span of the former having been increased twelve years during the past twenty, while that of the diabetic has increased sixteen in the same period. Operations hold no more peril for the diabetic in the hands of a competent internist and surgeon than for the non-diabetic; in fact, he usually goes through a less stormy convalescence than his so-called normal brother. It is doubtful if any drug has ever been introduced to the profession with greater care than insulin, resulting in a well trained group of physicians skilled in its use and in the treatment of the disease. So well has this instruction gone on that it can almost be said that the average internist of today has the knowledge of the expert of a decade ago.

Diet

While diet remains our sheet-anchor in the treatment of this disease, the results attained would be impossible without insulin. However, insulin without diet makes an impossible combination, the end-result being failure. Prior to the introduction of insulin, it was the exception to find a patient on a weighed or measured diet. The instructions to the patient included many "dont's" with regard to diet and usually as a sort of good luck charm allowed the use of gluten bread. Even today, it is rare to see a diabetic patient treated by the family physician, who has not been on a diet of which this bread is a part. It seems difficult for many to learn that the average gluten flour is not starch free or even nearly so and that the high protein contents forms a source of glucose. Gluten bread benefits the patient less than it does the manufacturer and baker. If the patient is able to take gluten bread, he is usually able to eat ordinary baker's bread. Prior to the use of insulin, little instruction was given to the patient regarding the nature of his disability, the calculation of his diet, elements of body chemistry, the prevention and emergency treatment of complications, etc., and quite naturally cooperation was rarely obtained, for why should one go to a great deal of inconvenience unless there is a good reason for it? Today the average diabetic is well schooled in these subjects as a preliminary to the treatment of his disease; in fact, many clinics maintain schools for the instruction of diabetics. Today the well trained patient is as conversant with "calories,"

*From the Laboratories of the Garfield Memorial Hospital, Washington, D. C.

*Read before the Osler Society, Washington, D. C., March 19, 1928.

"carbohydrate," "protein," "fat," "acidosis" and similar terms as many a physician. Filling a dietary prescription, examination of the urine for sugar and diacetic acid and for some blood sugar estimations are all in a day's work.

While it is our desire to teach our patients to think of the amounts of carbohydrate, protein and fat in grams and to be able to substitute a certain amount of one kind of food for an equivalent amount of carbohydrate, protein and fat, we must realize that there is a certain type of patient with whom this is impossible, due to lack of education. While the weighing of food is to be desired, except in the very mild diabetic, we are almost compelled to use substitute measures for these people. Here we can utilize the ordinary kitchen measuring cup and teaspoon to advantage with excellent results and obtain a satisfied and cooperative patient, where otherwise misunderstanding and dissatisfaction and ultimate loss of cooperation would follow.

There is no reason why any physician, who is willing to devote the necessary time and thought to the subject, cannot successfully treat this disease. Numerous charts, manuals and blank forms aid the physician of today in the effective care of his patient. The matter of diet has been made simpler to calculate than it was at the beginning of the insulin era. According to Allen at the recent meeting of the American College of Physicians, it is not necessary to calculate a diet according to the basal requirements of the patient, and the ketogenic and antiketogenic factors can largely be forgotten. The tendency at the present time is to get away from the high fat diets sponsored by Newberg and Marsh and to give more liberally of carbohydrates and protein. It now seems to be the consensus of opinion that large amounts of fat may be and probably are distinctly harmful to the blood vessels and more or less interfere with the regaining of a carbohydrate tolerance on the part of the patient. Joslin,[1] giving a minimum of fat and fairly large amount of carbohydrates and protein, has been able to carry his juevnile diabetics along satisfactorily with smaller amounts of insulin than used in many of the large clinics of the country. By gradually increasing the carbohydrate allowance of the patient, the tolerance can often be raised to a surprisingly high level and by a combination of this and insulin the patient's ability to utilize carbohydrate can frequently be raised from 50 to 100 per cent. With children we endeavor to give a diet approaching as nearly as possible that of a normal child for the same age. In 1925[1] the average diet per kilogram of body-weight given by Joslin in sixty cases contained 2.7 grams of carbohydrate, 1.9 grams protein and 3.4 grams of fat. He reports[2] the cases of ten children who began insulin in 1922. During a four year period following this, he has been able to double their carbohydrate, increase the protein one-half and the fat one-third, giving about 50 per cent increase in calories. Knowing that the amount of sugar in the blood is usually highest in the morning and lowest at night, we endeavor to include the greater portions of carbohydrate in the noon and evening meals. Occasionally the reverse will be found and breakfast would then receive the larger allotment of carbohydrates.

It has been our practice to give from 2 to 3 grams of protein per kilogram, the protein requirements being increased due to the increased metabolism in children.

Insulin

As stated before, it was impossible to obtain present-day results prior to the use of insulin and this drug has brought hope to all diabetics and happiness to many families where death would have taken its toll before. The increase in the age span of the diabetic is due largely to the prolongation and saving of the lives of children through the agency of insulin and intelligent treatment. As when it was introduced to the profession, insulin still remains a drug which if improperly used can cause serious trouble, and the physician who intends to make use of it should appreciate its potentialities for both good and evil. We find that we can keep our patients sugar free on smaller doses of insulin than previously, possibly by using less fat and more carbohydrate or by a more intelligent arrangement of insulin dosage. Where we formerly gave insulin before meals we now find that a fourth dose may at times be necessary, or, in place of a dose at supper, one several hours after this meal may better control the hyperglycemia which occurs usually between nine at night and breakfast. Allen recommends in some

cases to give the evening dose several hours after supper and the morning dose an hour or so before breakfast as a means of controlling this rise. We have known of several patients for whom it was necessary to give a dose at two or three o'clock in the morning. We have learned that smaller doses, not over 25 units at frequent intervals if necessary, are preferable to doses above this amount widely separated, as too great a fluctuation in the blood sugar is likely to occur.

While the blood sugar is usually estimated on samples secured in the morning before breakfast, after treatment has been started a better idea of the manner in which the food is being utilized can be obtained by drawing the blood specimens three hours after breakfast, in the late afternoon, just before the evening meal or occasionally between ten and twelve o'clock in the evening. Reports on blood sugar concentration at these various times will give one the knowledge of the variation during the day, usually highest in the morning and lowest at night. In young and middle aged patients a blood sugar of 160 milligrams per 100 c.c., three hours after breakfast is allowed, but in elderly patients amounts of 200 or even higher are frequently acceptable. If the renal threshold is normal, examination of four period specimens of urine—(1) breakfast to luncheon, (2) luncheon to dinner, (3) dinner to midnight, (4) midnight to breakfast—will give similar information and save frequent blood examinations. If the renal threshold is elevated to a considerable degree above normal (occasionally as high as 400 milligrams per 100 c.c.), blood examinations are essential, but we occasionally find a patient who does better by adjusting the diet and insulin according to our urine findings, rather than according to the blood sugar concentration. In elderly patients we must frequently be content to maintain the blood sugar concentration at a much higher level than we would in younger patients. We have seen cardiac distress complained of when the sugar in the blood was lowered by insulin to so-called normal levels.

However, we know that in an emergency, such as diabetic coma, 25 unit doses given subcutaneously and intravenously at frequent intervals are life saving and the formerly hopeless case can now usually be saved if observed and treated constantly over a period of hours, with frequent examinations of the blood and urine. If at all possible these cases should be treated in the hospital where frequent laboratory examinations are possible and all types of emergency treatment available. Diabetic coma demands the attention of the physician constantly until the acid poisoning is overcome or the patient dies. Usually it is possible to save a patient who has not been in coma more than twenty-four hours. With the increased knowledge concerning the treatment of diabetes, these cases are fortunately becoming rare. With the advent of insulin the use of bicarbonate of soda in this condition has become of less importance and in the hands of some is never used. One must not forget that a small percentage of acidosis is due to a retention of other organic acids than those involved in imperfect fat metabolism, and sodium bicarbonate is especially reserved for this type of case. After all, in this condition we are chiefly concerned with the degree of acidosis and not so much interested in the glucose content of the blood except to prevent its too rapid fall or a reduction below normal. For this reason it is perhaps well to use a certain amount of carbohydrate by bowel, mouth or vein in connection with the administration of insulin, although many cases of coma have been brought under control without the use of glucose, depending on the utilization of the excess glucose as evidenced by the high blood sugar. Eight to twelve hours' work and attendance on a coma patient, with the judicious use of insulin, usually rewards one with the knowledge that he has saved a life which would in all probability have been lost if insulin had not been available.

Operative procedures can be performed without fear, knowing that we can build up a carbohydrate reserve to be drawn upon as a result of the increased metabolic changes incident to anaesthesia. Patients are given carbohydrates and the necessary insulin up to three hours of the time of operation, and, if necessary, the introduction of glucose and insulin by vein can be continued during the operation and following operation. Postoperative acidosis need not be present if carbohydrates are given by bowel, vein or mouth with sufficient insulin to care for same, the blood sugar, carbon dioxide combining power of the blood and urinalysis being our guides

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for both insulin and carbohydrate therapy. Fluids are often as essential as either of these substances.

Infections and febrile reactions which previously were the starting points of acidosis and coma should cause us no more concern than the disease or condition at fault, as the patient is treated in exactly the same manner as the non-diabetic with the addition of sufficient insulin to take care of his needs. The diet is the diet of the non-diabetic. Frequent examination of the urine for sugar, acetone and diacetic acid, with occasional blood sugar estimations, will give information necessary to adjust the dosage of insulin. As feedings are often given every three or four hours, the frequency of the administration of insulin is usually increased.

By the use of insulin the carbohydrate tolerance of the patient can be raised to a degree not possible prior to the introduction of the drug. A certain amount of strain is taken off the pancreas by the use of insulin with a weighed diet, and it has been definitely shown that the islands of Langerhans regenerate and, as known for some time, many cases of diabetes originally classed as severe are found to be comparatively mild.

Exercise

Next to diet and insulin we feel that exercise is our greatest aid. This fact has long been known but could not be taken full advantage of until insulin made it possible for the patient to avail himself of this aid to its full extent. Muscular work burns up glycogen and raises the respiratory quotient. In the words of a patient of Joslin, "mental work makes sugar, muscular work burns it up." This is probably most apparent in children who are taking insulin. A schoolboy, who ordinarily takes from six to eight units of insulin on school days, will experience an hypoglycemic reaction due to the lowering of the blood sugar on Saturdays, when the day is largely devoted to play, unless the dose is cut to four or five units. Usually a mile walk or active play will represent the equivalent of several units of insulin. The value of exercise was demonstrated to one of us this summer while in Boston. There were seen a large number of diabetics treated by Joslin with relatively small doses of insulin plus exercise. If the patient was bed-ridden a trained attendant gave passive exercise with almost equally good results. In the same city another large group of diabetics were treated by diet, insulin and rest in bed and it was noted that the insulin dosage averaged considerably higher.

Newer Drug Therapy

Since the nature of diabetes was known, various drugs have been introduced in the treatment of this disease, but none achieved any success until the introduction of insulin. So far as the patient is concerned, insulin has the disadvantage of having to be taken hypodermically, it being ineffective by mouth, and this method, while acceptable to the majority, is strenously objected to by others.

In 1918, Watanabe[3] reported that guanidine was effective in lowering the blood sugar. These observations were verified by Frank[4] working with Nothmann and Wagner. In a discussion before the Society for Diseases of Digestion and Metabolism, Frank reported results secured with a synthetic substance, given the name "synthalin," and described as a guanidine derivative. This is essentially a compound consisting of two guanidine radicals attached through series of CH_2 groups. In synthalin there are ten of these groups. Subcutaneous injection in rabbits produced a fall in blood sugar and this action was also demonstrated in diabetic dogs. More than ordinary interest was manifested in this substance as it was found that the drug produced hypoglycemia when taken by mouth. The dose varies between 20 milligrams and 50 milligrams per day and is usually given as follows:

	Morning	Evening
1st day	20 milligrams	20 milligrams
2nd day	20 milligrams	
3rd day	20 milligrams	20 milligrams
4th day		
5th day	Same as 1st day, etc.	

The drug appears to be slower in action than insulin, and ordinarily from two to three days elapse before any definite lowering of the blood sugar takes place. Most observers consider that 1 milligram will cause an increase in glucose tolerance of 0.5 grams to 1.0 grams. In our experience we are inclined to favor the lower figure. After a period of from two to three days the insulin dosage can ordinarily be reduced approximately two units every other

day, the total reduction in dosage being largely dependent on the individual. After a period usually of several weeks, digestive disturbances occur, loss of appetite being noted first, followed later by nausea. Vomiting has not occurred in our series. These disagreeable symptoms can be avoided according to certain clinicians by the administration of various preparations containing bile salts. We and others have adopted the practice of either omitting the drug on the third day or every fifth day, stopping the synthalin for four days and increasing the insulin dose during this period. It seems to be the consensus of opinion that this preparation can replace up to 30 and 50 units of insulin and may allow the patient to reduce the number of doses of insulin from two or three to one or none daily. It should not be used in treating diabetes complicated with infections, acidosis or coma, and, if the digestive disturbances are not given proper attention, may give rise to acidosis from starvation. Its mode of action is not known, some reporting that it has no effect on the respiratory quotient, others that the latter is increased. Reports of an investigation by Blatherwick, Sahyun and Hill[5] on the effect of the drug when administered intravenously to animals showed it produced acute nephritis and liver damage. Horning[6] reports similar findings in dogs after the continued administration of synthalin by mouth and concludes that the toxic secondary phenomena experienced by humans must be due to liver damage.

Our own experience with its use in seven patients would indicate that:

1. In all except one it had a definite effect in lowering the blood sugar, and, as a result, the insulin dosage was decreased in six, two being able to discontinue the use of insulin at least temporarily, and one, a child, occasionally.

2. All experienced digestive disturbances during the course of treatment, and in two patients it was necessary to discontinue the use of the drug on this account.

3. Various liver function tests and urinalyses do not indicate that there has been any impairment of function of the liver or kidneys.

4. Hypoglycemic reactions are delayed or not experienced with blood sugars as low as 50 milligrams per 100 c.c.

5. In the cases of two children, the drug produced a definite lowering of blood sugar in one and in the other it was ineffective.

6. In view of its possible toxic action and its limited usefulness, we are hesitant in using it in all types of diabetic patients, particularly those with renal or vascular changes.

7. The drug appears to have been partially responsible for a considerable reduction in the dosage of insulin in six patients, from an average of 31 units to 12 units. The entire reduction could not be ascribed to the use of synthalin, as a regaining of carbohydrate tolerance was gradually being established in at least two of these patients; in the remainder, the greater part of the effect was thought to be due to the drug.

Table I shows the typical effect of synthalin.

In 1925, Durig, of the University of Vienna, impressed with the benefits reported among the diabetic peasants of the Alpine regions from the use of blueberry leaf tea, induced Wagner of his laboratory to undertake an investigation of its properties. He found two substances present, one tending to elevate the blood sugar, the other to lower it. This latter substance was isolated in rather impure form and named myrtillin. Its composition is unknown. Frederick M. Allen and Wagner have continued this investigation. It occurs in the leaves of all green plants and is present in relatively large amounts in the leaves of the blueberry and other plants of the myrtle family. Wagner has reported its presence in yeasts, bacteria and oatmeal. It is possible that it may be present in various organs of the body. Allen[7] states that the drug is unlike insulin chemically or physiologically, and suggests the possibility of its being a vitamine. It is now prepared in tablets of 0.325 grams (5 grains) each, one tablet being taken one hour before each meal, the total dose for the day being 1 gram (15 grains). Smaller doses than 1 gram daily are not as effective as that amount, but no greater benefit can be secured from larger doses.

The drug has no appreciable effect on the blood sugar level in rats and rabbits, but depancreatized dogs, who have a life expectancy following operation of about one week, have been able to live from twenty-four to sixty days, averaging from four to five weeks. In partially depancreatized dogs, they continue to live indefinitely if myrtillin is used, and

without this they die after a longer period than that experienced by totally depancreatized animals without treatment. In humans, the drug has a more inconstant effect, some being definitely benefited, and others (about 40 per cent) showing no change in the blood sugar.

Of sixty patients treated with myrtillin by Allen,[7] twenty-four showed no effect from the drug, and the remaining thirty-six were considered to have been definitely benefited, as evidenced by the ability to take more food or to decrease the insulin. Six patients were able to stop the use of insulin entirely. As with synthalin and other guanidine derivatives, hypoglycemic reactions in many cases, or in others delays it. As with synthalin, it appears to act best in the middle aged or those well along in years, although it has been of value in the treatment of some children and ineffective in some elderly patients. It will not lower the blood sugar below normal if used alone.

Our experience has been confined to its use in six patients. While the majority have not been taking the drug* long enough to evaluate its effect, we have thus far noted no toxic effects. In two cases a slight increase in tolerance was thought to have been brought about through the use of myrtillin.

Considerable attention has been paid to a

TABLE I

Miss. M. A. age 23, height 67 Inches

Date	DIET				Blood Sugar	Time	Insulin Units	Synthalin Mg.	Remarks
	C	P	F	Cal.					
1926									
June 12	103	57	104	1576	178	8 A. M.	64		Weight, 100 lbs.
June 17	103	57	104	1576	147	8 A. M.	68		Weight, 104 lbs.
July 8	93	55	104	1528	159	8 A. M.	68		Weight, 105 lbs.
Sept. 5	61	45	93	1261	146	8 A. M.	68		Weight, 120 lbs.
Oct. 10	84	56	92	1388	134	8 A. M.	68		Weight, 130 lbs.
Dec. 12	50	68	130	1642	139	8 A. M.	60		Weight, 138 lbs.
1927									
March 5	50	68	130	1642	90	8 A. M.	24		
May 8	50	68	130	1642	248	8 A. M.	32		Weight, 140.5 lbs.
June 26	50	68	130	1642	96	8 A. M.	30		Weight, 139 lbs.
July 29	60	68	120	1592					
Aug. 8	80	70	115	1635					
Aug. 13	90	70	115	1675	126	11 A. M.	30		Weight, 135 lbs.
Sept. 18	90	70	115	1675	152	11 A. M.	30		
Oct. 16	90	70	115	1675	100	11 A. M.	30	40	Weight, 134 lbs.
Oct. 17	90	70	115	1675			28	20	
Oct. 18	90	70	115	1675			24	40	
Oct. 19	90	70	115	1675			24		
Oct. 20	90	70	115	1675			22	40	
Oct. 21	90	70	115	1675			22	20	
Oct. 22	90	70	115	1675			22	40	
Oct. 23	90	70	115	1675	145	11 A. M.	22		
Oct. 24	90	70	115	1675			24	20–40–0	
Oct. 29	90	70	115	1675	50	3:30P.M.	20	20–40–0	
Nov. 5	90	70	115	1675	80	3:30P.M.	14	20–40–0	
Nov. 13	90	70	115	1675	55	3:30P.M.	8	20–40–0	Digest. disturb.
Nov. 19	90	70	115	1675	100	5 P. M.	8	20–40–0	
Dec. 2	90	70	115	1675	113	5 P. M.	8	20–40–0	Weight, 126 lbs.
1928									
Jan. 5	90	70	115	1675	72	5 P. M.	52	20–40–0	Broke diet during Christmas holidays. Weight, 132 lbs.
Jan. 7	90	70	115	1675			40	20–40–0	
Jan. 24	90	70	115	1675	105	5 P. M.	22	20–40–0	Icterus ind. 7.0. Weight, 132 lbs.
Feb. 5	90	70	115	1675	112	5 P. M.	20	20–40–0	
March 2	90	70	115	1675	118	5 P. M.	16	20–40–0	
April 4	90	70	115	1675	116	5 P. M.	16	20–40–0	Van den Bergh: neg. Icterus index 0.5.
April 24	90	70	115	1675			16	20–40–0	Weight, 130 lbs.

*Supplied by E. R. Squibb and Sons, New York City.

substance, glukhorment, sponsored by von Noorden.[8] The Horment Company, who are the manufacturers, assured Professor von Noorden that the substance was free from synthalin and other guanidine derivatives. British and Czecho-Slovakian investigators have subsequently shown that the material is either synthalin or some other guanidine preparation. In a recent address, von Noorden indicated that a hoax had been perpetrated and that the drug was evidently not the result of decomposition of pancreas as claimed by the manufacturers.

2. Diet, insulin, education and exercise are the most valuable aids in the treatment of diabetes.

3. Synthalin and myrtillin are effective by mouth in lowering blood sugar, but are not to be classed as substitutes for insulin in the present state of our knowledge. There is reason to believe that other and more effective oral therapy will be forthcoming.

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TABLE II

Summary of Results Obtained from the Use of Synthal'n.*

ADULTS

Case	Insulin		No. of Days	Digestive Disturbance	Final Disposition†
	From	To			
ADULTS:					
Mrs. B.	54	36	5	Yes	Discontinued
Mrs. H.	36	16	11	Yes	Discontinued
Miss K.	28	0	37	Marked	Discontinued
Miss A.	30	8	67	Slight	Continues drug
Miss S.	30	0	95	Slight	Continues drug
CHILDREN:					
W. D.	9	2	15	Slight	Continues drug
W. A.	70	70	150	Yes	Stops use of drug occasionally; mother feels that it prevents reactions.

*Supplied by Eli Lilly & Co., Indianapolis.
†Since this article went to press, the use of the drug has been discontinued in each case.

None of the drugs described for oral administration in the treatment of diabetes add anything of great value to the physician, and their only benefit can be to the patient, who may be relieved of one or more injections of insulin daily as a result of their use. They cannot be considered as true substitutes for insulin, and should not be depended upon or used in the presence of acidosis or infection. In other words, insulin still remains the drug of choice, although the recent advances in the preparation of such substances as synthalin and myrtillin give us hope that more effective oral therapy in this disease in place of the hypodermic use of insulin will not be far off.

CONCLUSIONS

1. Provided competent supervision and treatment is available, the age span of the diabetic should be as long as the non-diabetic.

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OPHTHALMIC AIDS IN GENERAL DIAGNOSIS.*

By HARRY E. PETERMAN, M. D., F. A. C. S., Baltimore, Md.

In preparing a paper for this meeting it has been my purpose to produce something that would be of interest and help to the profession in general. The subject I have chosen is a very broad one. A volume could readily be written about it and necessarily I must touch only some outstanding essentials.

During the last few years methods of diagnosis have become increasingly complicated, and the tendency has been to rely more and more upon laboratory tests, and to some extent neglect a careful examination of the eyes.

There are a number of external eye changes that are very significant in general diagnosis and I shall mention some of them briefly. In closing the eyes, lagging of the upper lids may cause a suspicion of Graves' disease; also a bilateral exophthalmos, unless it be quite marked, may be missed by the examining physician. Protrusion of one eye, even if of slight degree, is very noticeable and may result from several causes, such as tumor, abscess of the orbit, sinus disease, thrombosis of the cavernous sinus, or aneurism of the ophthalmic artery.

Recurrent subconjunctival hemorrhages in persons advancing in age are often an indication of arteriosclerosis. Puffiness of the eyelids may be due to nephritis or arsenical poisoning. Jaundice of the sclera indicates obstruction of the common bile duct, infection or sclerosis of the liver. Corneal scars or opacities indicate previous injuries or inflammations and, if bilateral and diffuse over the greater portion of the cornea, are generally the result of congenital syphilis.

Diplopia indicates a lack of co-ordination of the eye muscles, and if a finger or pencil is moved from side to side, up or down in front of the eyes, a paralysis or partial paralysis of one or more of the eye muscles can readily be observed. This condition suggests several possibilities in diagnosis. Syphilis perhaps claims first attention. Brain tumor, multiple sclerosis, meningitis, encephalitis are often causes of this condition. I have in my own practice observed three or four cases of diplopia with paralysis of one of the eye muscles (generally the external rectus, which is supplied by the sixth nerve) where it was caused by diabetes. In all these cases the diplopia and paralysis were promptly relieved when appropriate treatment was instituted.

Nystagmus is a spasmodic condition of the eye muscles characterized by rhythmic oscillations of the eyeballs. The movements may be horizontal, vertical or rotary. The discovery of this condition arouses a number of questions as to its cause. It may be congenital, due to defects of vision or albinism, or it may be acquired, such as found in miners, or may be due to labyrinthine pressure, or vestibular nerve irritation. It is frequently seen in multiple sclerosis.

Most medical men are quite familiar with the pupillary reaction, and in a general physical examination its reaction to light and accommodation is always noted. The size of the pupil in health varies with exposure to light and with accommodation and convergence. It is influenced by age, the color of the iris and the refraction of the eye. The pupil is a little smaller in old age, blue or gray eyes and in eyes with hyperopic refraction. The size and reaction of the pupil is also influenced by the action of certain drugs, ocular disease, where light perception is reduced, spinal or sympathetic lesions, localized cerebral lesions in special centers or tracts.

The pupil is dilated in ocular disease, such as glaucoma, atrophy of the optic nerve, or orbital disease, due to non-conductivity of light, mydriatic drugs, also in fright, emotion, anemia, vomiting, depressed nervous tone, aortic insufficiency, irritation of the cervical sympathetic, etc. The pupil is contracted in congestion of the iris, paralysis of the sympathetic, and also of the fifth nerve, in certain fevers, plethora, venous obstruction, mitral disease and under the influence of myotic drugs. All medical men are familiar with the Argyll-Robertson pupil (or reflex iridoplegia) where the pupil does not respond to light, but does respond to accommodation and convergence.

Unequal pupils are rarely seen in health and one must always keep in mind that a mydriatic may have been used. Inequality may also be due to difference in refraction of the eyes, lowered vision or blindness of one eye, traumatism or cerebral disease. Varying inequality of the pupils is considered a premonitory symptom of insanity. Rhythmical contrac-

*Read before the Baltimore City Medical Society, October 5, 1928.

tion and dilatation of the pupil occurring without alteration of illumination or fixation is known as "Hippus". This peculiar phenomena is sometimes seen in cerebrospinal sclerosis, neurasthenia, hysteria, epilepsy and in the early stage of acute meningitis.

Inflammations of the iris present a problem in which the internist and ophthalmologist may well co-operate in determining the cause. They are generally a manifestation of syphilis, focal infection or diabetes. The diagnosis of an iritis should be made carefully, and this condition differentiated from a conjunctivitis when the inflammation is local and confined to the conjunctiva; also from glaucoma where the inflammation involves the deeper structures. Iritis is characterized by a medium or small pupil, early tendency to formation of posterior synechia with pigment proliferation at the pupillary margin. The iris soon changes in color and has a muddy infiltrated appearance; the gray iris becomes greenish in color. There is circumcorneal injection and the eye usually has marked ciliary tenderness.

In glaucoma the pupil is usually dilated, and does not react well to light. The tension is noticeably increased, especially in the inflammatory varieties when the cornea is steamy and the vision blurred. In conjunctivitis the inflammation is confined to this structure and the pupil remains active; there is no changed color of iris and the vision is unimpaired. A proper diagnosis between these conditions is most essential, especially between iritis and glaucoma. In iritis it is most necessary to use atropine to dilate, and keep dilated, the pupil, while in glaucoma eserine or pilocarpine is used to contract the pupil, and in many instances will rather promptly relieve the pain and other acute symptoms of the disease.

To make the mistake of using atropine or any mydriatic drug in glaucoma is always a serious one, as it promptly aggravates the condition, increases all the symptoms and sometimes causes the loss of vision. I have gone into this condition at some length for the reason that we are occasionally seeing cases where this mistake has been made.

Opacities of the cornea are always noted. They may be the result of wounds of the cornea, ulcerations or inflammations, or may be the remains of deep inflammations resulting from the interstitial keratitis of inherited syphilis. When they cover any part of the pupillary area they interfere with vision to a lesser or greater extent.

The visual fields are helpful in diagnosis when they are defective. The normal field of each eye extends temporally 90°, nasally 60°, above 55°, below 70°. The fields for colors, of course, are much less in extent, blue, red, green, respectively, in size. The visual field is soon affected in cases of glaucoma; the contraction is general but most marked in the nasal field, and in many instances, unless the condition is controlled, the contraction in the nasal field continues until it involves the central fixation point, when, of course, useful vision is lost. Hemorrhages or exudates in the fundus produce a blind spot in the field corresponding to the area of their location. A lesion in the right or left optic tract back of the chiasm will produce a *hemianopia* or half vision. If it is located on the right side it will blot out the nasal field of the right eye and the temporal field of the left eye and *vice versa*. If a lesion be located in the chiasm, the function of the decussating fibers to the nasal side of each retina will be cut off and the opposite fields, temporal fields, will be blind bi-temporal hemianopia. If the lateral fibers of the optic tract on both sides of the chiasm be co-incidentally involved, the temporal halves of the retina would be cut off and a bi-nasal hemianopia would result. A lesion such as traumatism or pressure on the nerve located between the chiasm and the eyeball will produce blindness of that eye.

In conditions where the sinuses are affected, the blind spot is often altered and enlarged and central vision may be reduced by the appearance, first, of a relative, and, later, an absolute scotoma. The above conditions are also often met with in cases of neuro-syphilis, traumatism, hemorrhages, intra-cranial pressure due to tumors and other lesions, and a careful mapping of the visual fields will be a great help in the diagnosis.

Careful examination of the eye-grounds generally is a great help in diagnosis, and this is accomplished by use of the ophthalmoscope. The use of this instrument is no longer confined to the ophthalmologist but is very generally used by medical men, especially by the internist and psychiatrist. The invention of the electric ophthalmoscope has to some ex-

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tent simplified its use and most medical men can use it and get some help in diagnosis from it.

In the use of this instrument one must naturally at first thoroughly familiarize himself with the appearance of the normal fundus, as it is often a question whether changes or different conditions are physiological or pathological. With this instrument one is able to see and recognize changes in the crystalline lens, vitreous humor, the condition of the optic nerve head or papillae, the blood vessels: also, to see hemorrhages and exudates, tumors, detachments of the retina and occasionally foreign bodies. Most of these conditions are manifestations of other body changes and diseases and the change in the eye is only a local manifestation of the disease.

Changes in the optic nerve head or papillae may be a change in color anywhere from a pallor to a distinct atrophy. There may be congestion, indicating a low grade of inflammation, or this may be more severe with swelling, indicating a definite optic neuritis, and this may be still more pronounced, indicating a definite condition of choked disk. The margins of the disk may be clear cut, or in low grade inflammations they will be indistinct and sometimes fade into the surrounding retina so that one cannot tell where nerve ends and retina begins.

Most all of you are familiar with the picture of a choked disk, always indicating an abnormal intra-cranial pressure. Brain tumors sooner or later, due to pressure, cause choked disk. This condition may also be produced by brain abscess, meningitis, fracture of the skull, sinus thrombosis, gummata, etc. Sometimes it is a fairly difficult matter to definitely say whether you have a choked disk or an optic neuritis. The essential points of difference are, in choked disk the veins are very full, usually tortuous while the arteries are small and contracted. In optic neuritis the arteries are usually normal and the veins full. The elevation of the nerve head, due to the swelling in choked disk, is usually much greater than in optic neuritis. The vision in optic neuritis usually becomes impaired (central scotoma) early in the disease, while in choked disk it may remain normal or nearly normal for a long time.

Changes in the blood vessels are always looked for and noted. No where else in the body can the blood vessels be seen so clearly, and here they are very accessible for direct observation. The changes in the vessels themselves are so prominent that they often explain definitely a clinical picture. Changes are to be noted in the caliber of the vessels, contractions, dilatations, differences in the proportionate caliber of the arteries and veins. Changes in color should also be noted, such as accompanying white stripes, transformation into white cords, and infiltrates in and over the vessels. Also to be noted are the number and arrangement of vessels, their course—whether tortuous, wavy or broken, the reflex, its breadth and intensity, also the phenomena of pulsation.

Pulsation of the retinal veins is considered a normal phenomena and is most distinctly seen on the disk where they descend into the normal physiological excavation. The retinal arterial pulse is always to be regarded as pathological. It indicates either an abnormally high blood pressure, high pressure wave in the arterial system, as in cardiac hypertrophy, aortic insufficiency, aneurism of the aortia or carotid, or an abnormally low blood pressure, as after great loss of blood, syncope and, finally, in glaucoma due to increased intraocular tension.

I wish now to consider some changes as seen in the retina and choroid, namely, hemorrhages, spots, exudates and pigment changes. The nutrition of the retina is derived from two sources: the central artery of the retina supplies the inner or cerebral layers, while the outer nerve layer and pigment epithelium is supplied by vessels from the choroid. This blood supply is of some clinical importance for the reason that it helps to determine finer points in diagnosis. The appearance of pigment stains or accumulations of pigment in the retina would indicate disease of its outer layers or of the retina and choroid, such as a chorioretinitis, while changes in the retina without involvement of the pigment indicate involvement and disease of its inner layers.

Hemorrhages are possibly the most important of the changes in the retina, and when injuries, glaucoma or high degrees of myopia are excluded, they are always considered to be a sign of general disease. They are a signal of warning that something is out of order in the system and a very careful general examina-

tion is demanded. Hemorrhages may be very small, such that they can only be detected through the dilated pupil and direct method of examination, or they may be large and massive, making the fundus look almost like a lake of blood. Usually fine striped hemorrhages which radiate from the papillae lie quite superficial, while round or lumpy ones are more generally in the middle or deep layers. The location of hemorrhages should be noted, their relation to the papillae, the macula and to the large vessels, or whether they are in the vitreous. Small hemorrhages come from the capillaries while large ones come from the larger vessels. It is impossible to differentiate between a venous and an arterial hemorrhage. Hemorrhages of a bright red color are recent ones, while older hemorrhages are usually of a dark or brownish tint.

The absorption of hemorrhages takes place slowly and they often disappear without leaving a trace as to their location. Occasionally white spots or pigment traces remain to tell their location. Isolated hemorrhages in the macula region are usually arteriosclerotic in origin if they are not due to traumatism or high myopia. Small shuttle-like hemorrhages that have a white spot in the center are generally caused by diseases of the blood, such as anemia and leucocythemia.

Among the principal causes of retinal hemorrhage, the one that should be mentioned first is traumatism, such as contusions or wounds. They are also found after body injuries, such as compressions of the thorax. One of the most important causes of retinal hemorrhage is arteriosclerosis and in these cases they are of great prognostic importance as they are often forerunners of cerebral hemorrhage. Nephritis and diabetes are very important causes both of small and large hemorrhages, and these hemorrhages usually appear at the same time with white spots.

In the case of nephritis the spots are white fat-like deposits and are generally arranged in the macula region in the shape of a star-like figure. Diabetes can, and often does, produce a picture quite similar to that caused by nephritis because the anatomical basis of the change is the same. Syphilis is also a cause of retinal hemorrhage, but other manifestations of this disease are always present and contribute most in making a diagnosis. Diseases of the blood, as previously mentioned, anemia and leucocythemia, are causes of retinal hemorrhage. Hemorrhagic diathesis as well as purpura and scurvy occasionally cause retinal hemorrhages; also, they are occasionally seen in the acute infectious diseases, such as malaria, typhoid fever, influenza, etc.

A very striking picture of the eye-ground is produced in occlusion or thrombosis of the central retinal vein when the hemorrhages are many, large and striated, covering up many of the blood vessels and other details of the fundus. In striking contrast to this picture is the one seen when there is an occlusion or thrombus of the central artery of the retina, where the retina is ischemic, some edema present, blood vessels, especially arteries, small or obliterated, and there is present a cherry red spot in the macula region. In the former condition of occlusion of the central retinal vein, the vision is usually very greatly reduced, but in many cases useful vision may be retained, while in the latter condition of occlusion of the central artery of the retina blindness is complete and comes on very suddenly. A few cases of this latter condition are reported when a small sector of vision was retained due to blood supply from a cilioretinal artery.

The vascular supply of the choroid is through the so-called ciliary vessels which come from the ophthalmic artery. The venous outflow from the choroid is quite different from its arterial supply, as its veins carry away not only the blood from the choroid itself, but also that from the ciliary body and iris. In pathological changes in the choroid we see changes in the blood vessels, pigment changes and spots similarly as I have described in the retina. Practically all diseases of the choroid are symptomatic of general disease with the exception of those that are congenital or due to myopia or traumatism. If white spots or black pigment changes are present, a thorough examination should be made and this should include a Wassermann and tuberculin test. If sclerosed vessels are present in the choroid, the probable cause of the disease is either syphilis, arteriosclerosis or nephritis.

Many of the signs and symptoms as revealed by a careful examination of the eyes are definite and point to an exact diagnosis, while others are only clues to be followed up and proven or disproven by further study.

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PREVENTION WILL BE THE WATCH-WORD.*

By J. L. EARLY, M. D., East Radford, Va.

Before presenting the subject of this paper, I wish to express to the Southwestern Virginia Medical Society my appreciation of the honor conferred upon me in being selected as your president for the past year. I wish to thank our very efficient Secretary-Treasurer, Dr. E. G. Gill, and the various committees for the assistance given me, and to assure the whole Society of my appreciation of their support.

According to figures compiled by the Public Health Service and of the American Red Cross, illness brings to the physicians of the United States $1,500,000 daily. A survey of 1,200 families, by the Department of Labor, reveals that the average annual expenditure for illness was $60.00.

There are $5,000,000,000 worth of hospitals in the country and their daily maintenance is $3,000,000. Two per cent of the population are incapacitated by illness and more than half are suffering from some kind of ailment.

The answer to the high cost of sickness in the United States is prevention, which must be elevated to the same plane as cure. Although the American public is emphatically aware of the startling improvements in such fields as aviation and television, to name only two of the many spheres of scientific progress, few persons realize more than vaguely the gigantic stride which medical science has taken in the last century.

Medicine, once an art, is now not only a science but daily an increasingly exact one. Disease, the dread enemy of a thousand years, is at last beating a retreat before the combined forces of research and experimentation.

A hundred years ago, even fifty, smallpox was a scourge, which swept away great numbers of people. As such it was accepted and its treatment, if such it could be called, was empirical at best. Today, due to the almost universal adoption of vaccination, smallpox is a rarity, found only in isolated, ignorant communities.

Cholera, once brought to ports by sailors from foreign shores is even more rare than smallpox, due to health laws, rigid sanitation enforcement and quarantine examinations of all incoming passengers and crews.

Another retreating figure of distress and sorrow, not yet wiped out but distinctly on the wane, which has claimed its millions among children, is diphtheria, now preventable by inoculation.

Scarlet fever, measles, mumps, tonsillitis, croup—all fearsome diseases of childhood—stand at bay before either improved methods of cure or prevention.

Among adults, such complaints as diabetes, now successfully treated by insulin and a regulated diet, whereas it was formerly usually fatal, and rheumatism, now recognized to have in each case an individual underlying cause requiring individual methods of treatment rather than a shrug of the shoulders and a resignation to fate, are fast being conquered.

When grandmother caught a cold, she let it go at that, but today colds are known to have as many causes as there are hairs on grandson's head and are cured or alleviated accordingly. Some colds are, as it was formerly supposed all were, caused by sitting in a draft, but, among reputable physicians of the present day, it is held with conviction that a cold is more apt to be caused by wrong diet, or improper health surroundings, or by inhaling the germs shed by some one already infected, than by "bad night air" or a severe cold. Another cause of colds now generally accepted in step with the spirit of modern times and dress is the wearing of too much clothing or the use of too many bedclothes at night. Colds are now treated more and more by resting, and sleep and diet correction, rather than by patent medicines and the "physic" and "home remedies" so beloved of yore.

It is possible that in the future, by the proper regulation of diet of both mother and child, the extensive loss of teeth in children and the diseases causing their decay will be eliminated. The question of diet, so long the subject of feminine conversation and query, is more accurately understood than ever before. It is recognized that each individual requires an individual diet. By means of blood chemistry, an embryonic but apparently revolutionary branch of medical science, a man's blood, blood pressure and urine are subjected to a more defined and exact analysis than ever before.

Surgery is now safer, not only because of the improved antiseptic facilities, but also because surgeons know better how to operate. More things are now accomplished by modern surgeons than the early and middle nineteenth

*President's address before the Southwestern Virginia Medical Society in Wytheville, September 27-28, 1928.

century disciples of Hippocrates ever dreamed would be. Appendicitis operations are no longer a bait for joke magazines, nor are they viewed with mid-Victorian terror, but are recognized, except in acute and neglected cases, as necessary life-saving operations. The public realizes that millions formerly died of disease and conditions now cured by the surgeon's knife.

Eyesight is improved and blindness prevented by modern eye surgery and the entire body is subjected to the scapel with beneficial results. The World War experiences have added immeasurably to the known results in facial surgery and bone and jaw relineation.

Perhaps the greatest advance in modern medicine is in the field of diagnosis. Diagnosis, now as mentioned before, closely allied to blood chemistry, calls for even more than that; it means today that if a person is suffering from some apparently local complaint, such as stomachache, a headache, or neuralgia, his symptoms of pain, fatigue and what not are of course thoroughly gone into, and his whole body is subjected to a thorough examination by experts in each portion of it. Particular attention is paid to his eyes, teeth, digestive tract, and his medical history.

The chief problem of the future in medicine, save for the stamping out of known dangerous diseases and the prevention of new ones, is the prolongation of human life. To this end alone —after all, the chief one of the medical profession—millions of dollars and years of time, as well as tons of brain, sinew and struggle are being devoted by countless quiet unassuming scientists and physicians, who work silently but persistently for the good of humanity and the glory of science. In line with the general improvement of medicine in all of its branches is the constant campaign being urged by the American Medical Association and many other physicians and societies to enlighten the public, keep it healthy, and prevent recourse to the many charlatans and quacks who, quick to seize upon a man when he is ill, defraud him of his money and shorten his life. And hand in hand with medicine's advance, the public's increase in common sense has marched.

Elbert Hubbard has said, "That ignorance and sin supply the three learned professions their excuse for being." Certainly physicians are daily faced with ample evidence that ignorance of hygienic laws and some of the results of sin create the illnesses we are called upon to treat. As sin and ignorance disappear from the world, so too will the need of our services be lessened each decade. It is possible for us to conceive of our society progressing to the extent where sin and ignorance are practically extinct, as are witchcraft, slavery and torture. In such society there would be very little need for members of the three learned professions. When business men stifle their greed and cease to squabble, the lawyer finds his work gone. When man understands God, the need of a professional interpreter diminishes and when folks are fully educated on matters of health and hygiene, when laboratories have wiped out disease and plagues, then our work in mending and treating and curing shall have ended.

This is, of course, in the far distant future. Society though has made more progress in that way in the last ten years than in the last thousand. Enough progress has been made that a certain per cent of the ailing public no longer ails. In a world which no longer needs the lawyer, clergyman or doctor, the teacher will still be needed. Teachers not only of language, mathematics and chemistry; not alone of music and arts; not alone of the graces —but teachers of health.

The physician of the future will be not only a curer of the sick but a teacher of health.

Preventive medicine will be the vogue. Prevention will be the watchword.

THE INCIDENCE OF INFLUENZA AT BLUE RIDGE SANATORIUM DURING THE EPIDEMIC, DECEMBER AND JANUARY, 1928-1929

By
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and
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As the present influenza epidemic began to spread and get near, we realized that every precaution should be taken to prevent its spread among the personnel and patients of the institution. It is a well known fact that during the epidemic of 1918-19 the morbidity as well as the mortality of tuberculosis was increased. Also, we realized that the institution represents an educational factor in the public health problem and we were especially anxious that the lowest possible incidence should occur.

With these points in mind, the nurses and

employees were advised to stay away from Charlottesville just before and during the Christmas holidays as it was reported that there were about fifteen hundred cases there during that time. In a talk to the colored employees they were especially urged to stay away from crowds or places where influenza was present and instructed to cover the mouth and nose with a handkerchief when coughing and sneezing. The patients were assembled and a talk given them on how the disease is spread and the prevention of it was gone into in detail. They were advised to urge upon their relatives and friends not to visit them until the epidemic was over. Shortly following this the patients were again talked to on this disease and the former points further emphasized, and in addition to this they were given a leaflet provided by the State Board of Health headed, "Protect Yourself and Others Against Influenza," this leaflet to be sent with their mail to the relatives and friends throughout the State. Large placards were made which had printed on them the methods necessary to prevent influenza and posted throughout the buildings of the Sanatorium. All visitors to the Sanatorium before being permitted to see the patients were seen in person by a nurse or doctor and questioned closely as to whether they had been exposed to influenza or if they had at the time a cough or symptoms of a recent cold.

Patients have been admitted all the time during the epidemic but have been isolated for four or five days after admission. None of these cases, we are glad to say, developed the disease.

Of the thirty-two cases we have had here, twelve have occurred among the staff and nurses; four in the white employees; nine in the colored employees, and seven in the patient body. The cases occurring in the patients have been traced to a visitor on Christmas day who was said to have had a mild attack. It is gratifying to know that the training that has been given the patients in preventing the spread of spit-borne diseases has produced such good results during this epidemic. Only 2.6 per cent of the patients so far have contracted the disease.

Symptoms

The symptomatology varied some but as a whole was as follows: The onset was acute in most cases, though in a few cases listed as slight in the table, it seemed to be gradual. The subacute cases being mostly the ambulant form, the symptoms were not so easily recognized. In the cases with acute onset there was usually noted at first a burning, dry and raw sensation in the pharynx and trachea. This was soon followed by a dry non-productive cough accompanied by a sensation of constriction and pulling in the substernal region. This was thought to be due to a tracheitis. There was also generalized aching with a preference for the back and head. Within a period of six hours, as will be noted by the temperature curves, the temperature rose from one to three degrees on day of onset and continued to rise until in the moderate and severe cases it reached 102 to 103 on the second or third day. At this point it began to decline until on about the eighth day it was normal. The curve of the temperature all along shows the highest readings in the afternoon and evening, except on the fourth day when both groups showed a drop in the evening. Following the onset the cough soon became productive and the constriction and pulling in the region of the trachea and bronchi were lessened. The appetite was poor from the onset until convalescence became established; especially, late in the disease there was a distaste for food and water. There was no diarrhea and very little constipation. Three cases had some vomiting on the first and second day when temperature was at its height. Aside from these the patients were comparatively free from gastro-intestinal disturbances. No central nervous system disturbances were noted. Urinalyses were not done on all of these cases, but were within normal limits on those done.

Unfortunately, complete blood work was not done on all the thirty-two patients listed in this report and is not available for complete study. However, we do feel that the work listed in the table is of definite value and brings out certain important features. Of the seven tuberculous patients in the Sanatorium who had influenza, complete blood work was done before, during and after the attack. In addition to these, three nurses had blood work done on them during the disease and within eight to ten days after. Thus there are listed seven cases having had blood work done on them before the disease and ten cases during third or fourth day of attack, and the same ten cases with blood studies repeated dur-

ng convalescence. To make this work of greater value it may be added that the entire list including patients and nurses either have tuberculosis or are strongly suspicious.

An analysis of this work reveals the following: Hemoglobin dropped during the disease 1½ per cent but during recuperation there was an increase of 2½ per cent over that observed during the height of the attack. The total white cell count harmonizes with the reports of other observers; namely, that there is a decrease in the number of leucocytes. Only two of the cases had a total white count to exceed 10,000 and one of these occurred in the pneumonia patient, the other in a case of artificial pneumothorax who had pleural effusion previous to the influenzal attack. Had these cases been omitted there would have been a more noticeable decrease in the white cell count during the course of the disease. In spite of this there was a reduction of almost 1,000 cells during the attack which was not regained during recuperation. In the differential count there was a fall of 7.5 cells in the polys, and while this was slightly increased during recuperation it did not get back to what it had been previous to the attack. The small lymphocytes showed a slight increase and continued to rise during convalescence. The large lymphocytes showed an increase of about 3 cells during the attack, but unlike the small lymphocytes they showed a decrease of eight or ten days after the influenzal attack. Perhaps the most noticeable change in the entire work was seen in the transitional count. These cells were increased from 1 per cent before to 4.5 per cent during the disease, but rapidly approached the point of normalcy during convalescence. The eosinophiles showed a slight reduction and this was not regained afterwards.

It may be inferred from these results that there is a reduction in hemoglobin, white blood cell count and polys during an attack of influenza in tuberculous individuals. However, the small and large lymphocytes, and the transitional cells show an increase. Whether it is a coincidence or of definite clinical significance it is noteworthy that the small lymphocytes continued to rise during convalescence. It is now believed by some observers that the lymphocyte count represents a clinical index to the resistance of the patient with tuberculosis. Cunningham, Sabin, Sugiyama and Kindwall (Transactions of the Annual Meeting of the National Tuberculosis Association, 1925 and *American Review Tuberculosis*, June, 1928) found by inoculation of rabbits, and later confirmed on patients, that in progressive tuberculosis the number of circulating monocytes (transitional cells?) increased and the number of the lymphocytes decreased. They found the reverse to be true when the animals were recovering. If this work of Cunningham, *et al*, be correct it would seem that our observations are of some definite value and it would be of interest to make further studies on a larger series of cases. It would be extremely interesting to compare this feature of the blood work with observations made on non-tuberculous individuals who had influenza.

BLOOD WORK TABLE

On Admission	Hb. %	W. B. C.	P. M. N. %	S. L. %	L. L. %	T. %	E. %	B. %
Seven cases	83 2-3	8,640	74	19	6	1	1 1-3	0
During Influenza (3rd to 4th day of attack) Ten cases	82 2-9	8,000	66 1-2	20 1-2	8 2-3	4 5-12	7-10	0
Recuperating. (8 to 10 days after influenza) Ten cases	85	7,400	69 3-10	22 4-10	7 1-10	1 7-10	4-10	0

Complications and Sequelae

Complications and sequelae occurred in seven of the influenza cases. This is 21¼ per cent. The most serious complication listed is pneumonia. This was of the bronchopneumonic type, of which one patient had a definite diagnosis, while four had a symptomatology highly suggestive. These are listed in the table as suspicious of bronchopneumonia.

The most serious sequela which occurred was relapse. This took place in two patients.

In addition to relapse one of these patients had acute bilateral antritis with epistaxis. (It might be of interest to know that this patient had arterial hypertension before developing influenza). The second attack of influenza in both patients was more serious than the first attack. One patient had as a sequela acute otitis media. Pleuritis occurred in one patient who was under treatment as a suspicious case of tuberculosis. It is of interest to note that of the seven patients in the Sanatorium under treatment for tuberculosis only one is listed in this group of complications and sequelae; the others being employees and personnel of the institution.

General Tabulation of Influenza Cases at Blue Ridge Sanitorium, December and January 1928-29

Patients	Mild (1-3 da.)	Moderate (6-10 da.)	Severe (6-10 da.)	Complications and Sequelae	Onset — Acute	Onset — Sub-acute	Sex M.	Sex F.	Tuberculosis or other prev. disease
Staff and Nurses.....12	1	9	2	Bronchopneumonia.....1 Suspicion of Bronchopneumonia.....2 Otitis Media, acute.....1	10	2	11	1	Pulmonary T. B. Susp.....1 Min.....4 Mod. Adv.....2 Bronchiectasis 1
White Employees.....4	3	0	1	Susp. Bronchopneumonia.....1 Marked Relapse, with acute bilateral antritis and epistaxis..1	1	3	4	0	Mitral regurgitation and stenosis.....1 Arterial hypertension.....1
Colored Employees.....9	3	4	2	Marked relapse, with susp. Bronchopneunonia.....1	8	1	9	0	Diabetes mellitus.....1
Patients in Sanatorium..7	4	1	2	Pleuritis.....1	4	3	6	1	Susp. T. B.....2 Mod. Adv.....3 Far Adv.....2
Total.....32									

NOTE: Three people living on farm, not employees, and not listed here, had "flu."

Treatment

The general treatment given these patients was to put them to bed as soon as the symptoms appeared and keep them at rest until at least two or three days after the temperature had become normal. Fluids were forced. Liquid and soft diet were given with an abundance of fruit juices. Sodium bicarbonate in twenty to thirty grain doses was given in a glass of water every three or four hours during the first two days to alkalinize the body fluids. Aspirin, grains ten, was given every three hours if aching was present and in some instances a dram of Aromatic Spirits of Ammonia was given with it. Cough sedative (mixture of Ammonium Bromide, Syrup Squill, Flext. Pruni. Virg. in simple Elixir) was used in doses of drams one every three hours for the cough.

Comments

Of the total number of cases twelve, or 37.5 per cent, were females, and twenty-one, or 62.5 per cent, were males. Of the seven patients in the Sanatorium having the disease six were males and one female. All listed under white employees were males. Also, all listed under colored employees were males. Under staff of the eleven listed, there were ten females and only one male. It is significant that none of the forty children in the institution had the disease. The average age instance is as follows: males, thirty-three years; females, thirty-two years. Of the males the youngest was seventeen years old, while the oldest was fifty-five years. Of the females the highest age limit was forty-two and the lowest twenty-two. Of the total number cases, fourteen or 43.4 per cent either had definite pulmonary tuberculosis or were

considered as "suspicious". Other diseased conditions existing before onset of influenza were: diabetes mellitus, one; arterial hypertension, one; mitral valve disease with cardiac hypertrophy, one; bronchiectasis, one.

Conclusions

1. From these observations in a limited number of cases it would seem that influenza occurring in tuberculous individuals who have high resistance as a result of Sanatorium treatment, get good results and are not done harm to any appreciable extent, if required to remain in bed for a fairly long period during convalescence.

2. There seems to be a characteristic temperature curve in this epidemic of influenza. On the day of onset the temperature rises from one to three degrees and continues to rise until it reaches 102 to 103 degrees on the second or third day in mild and severe cases. No exception was noted to this in tuberculous patients who were improving and otherwise doing all right.

3. As no controls were run it is not possible to say just what effect the administration of alkalies had. The standardized use of alkalies with salicylates in the treatment of influenza seems to be equally as efficacious in tuberculous individuals having the disease.

4. Of the blood work done on the small number of cases all having tuberculosis, the noticeable features were: leucopenia, reduction in polymorphonuclears to the extent of 10 per cent, and a definite increase in small lymphocytes which continued during recuperation. The large lymphocytes were slightly increased and what seems to be a noticeable feature is the increase in transitional cells (monocytes). These during the attack were increased three and one-half times.

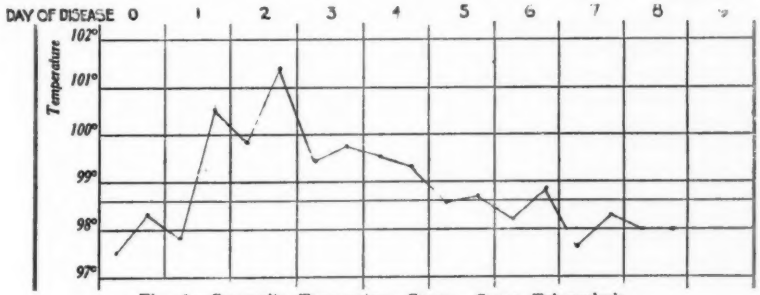

Fig. 1.—Composite Temperature Curve. Seven Tuberculosis Patients.

5. Influenza is a spray-borne disease and the spread of it can be prevented by observing the two rules as advocated by the State Board of Health; namely, "Cover the mouth and nose with a handkerchief when sneezing and coughing, and keep objects such as, pencils, fingers, etc., which do not belong there out of the mouth". It was through these precautions and in addition to these, isolation, that there was a low incidence of influenza at Blue Ridge Sanatorium during the recent widespread epidemic. Only 2.6 per cent of the two hundred and seventy patients, and only 8.5 per cent of the entire Sanatorium

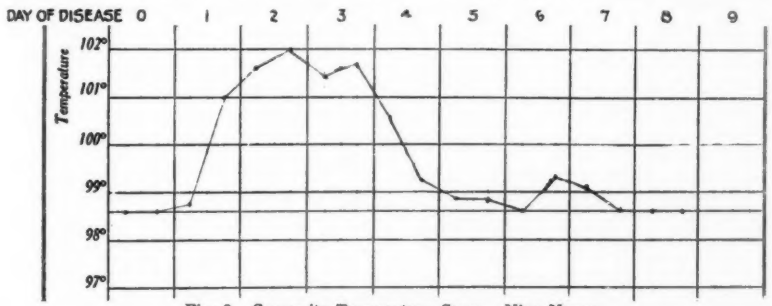

Fig. 2.—Composite Temperature Curve. Nine Nurses.

community, including patients, staff and employees, developed the disease.

Of the staff and employees 23.8 per cent developed the disease. It must be borne in mind, however, that they were exposed to the public more and were unable to protect themselves against the infection.

ANGINA PECTORIS.*

By K. D. GRAVES, M. D., Pearisburg, Va.

It is often profitable as well as interesting to take inventory of the facts and theories pertaining to certain diseases, in order to take advantage of any available information pertaining to them. It is with this purpose in mind that I approach the subject of angina pectoris.

The nomenclature is misleading, as all descriptions of the condition first state that it is a symptom rather than a disease entity; and then further qualify by ruling out the majority of cases of heart pain.

The symptom complex of angina pectoris occurs more frequently in males than females, in white than colored persons, and practically never in persons under forty years of age. It is always serious. It is rapidly increasing, as is shown by the following tables:

TABLE I.
Death Rate From Angina Pectoris in Virginia, Per 100,000

Year	White	Colored	Total
1923	11.24	6.16	9.34
1924	11.03	8.00	10.14
1925	11.96	8.56	10.94
1926	12.64	8.88	11.51
1927	13.78	11.13	13.04

TABLE II.
Death From Angina Pectoris per 100,000, All Ages, Metropolitan Life Insurance Co., Industrial Department

Year	White Male	White Female	Colored Male	Colored Female	Total
1923	7.0	4.7	5.7	6.1	5.7
1924	7.5	4.2	5.3	5.6	5.7
1925	8.1	5.1	6.7	7.2	6.5
1926	10.7	5.9	8.1	8.3	8.0
1927	11.4	6.2	8.4	7.8	8.4

It is very possible that these tables may be slightly misleading, as Mr. Dunbar, statistician for the Metropolitan Life Insurance Company, in a personal communication states that he considers that the increase is partly due to the fact that there is a tendency on the part of doctors to attribute deaths to angina pectoris which formerly have been classified as being due to acute indigestion.

The term does not include the heart pain in young persons, lasting from a few minutes to several days, never extremely severe, rarely dangerous, often relieved by exercise. I have been unable to find that young persons subject to such attacks are predisposed to attacks of angina vera. The term should include only cases having a feeling of constriction or oppression in the chest, great apprehension and a feeling of impending dissolution; with pain often excruciatingly severe, usually in the precordium but often in the abdomen, shoulder or elsewhere.

We would usually find it extremely difficult if not impossible to make a diagnosis of angina pectoris except for the subjective symptoms. Electrocardiographic studies are frequently negative, and at best are usually only suggestive rather than confirmatory. There are no consistent postmortem findings. Percussion, auscultation, palpation, and blood pressure readings are of little help. Because of the variability in objective findings considerable speculation has taken place over the mechanism of angina pectoris. Sir Clifford Albutt has taught for a long time that it is due to aortitis, and probably has nothing to do with heart disease. The theory which many of us learned at college, that it was due to constriction or blockage of one or more of the coronary vessels has lost adherents, owing to the wide variety of autopsy findings on these cases. Another theory is that it is due to a spasm of the coronary arteries, causing a local ischemia of the myocardium. The explanation of Reid[1] is fast gaining adherents, viz., that it is functional in the same sense as are the arrhythmias. Ordinarily, during exercise there is a dilatation of the peripheral blood vessels, thus draining the blood away from the heart. In Reid's opinion, angina pectoris may be due to failure of the peripheral vessels to dilate, thus causing a sudden rise of pressure of the first part of the aorta and the left ventricle. It is easy to explain by this theory how the vasodilators, such as the nitrites, afford relief.[2]

Treatment may be divided into medicinal

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and surgical. In the realm of drugs, the nitrites are probably unsupplanted. A number of operations have been devised, probably cervical sympathectomy being the most popular. At present, surgery is invoked usually only in cases of unbearable suffering: it affords relief to cases which survive it, but it is considered a last resort rather than a first resort. It is very possible that as surgery becomes more frequently resorted to, it may eventually be elaborated to such an extent that it will afford functional as well as symptomatic cures.

I wish to express my indebtedness for the statistics to Dr. W. A. Plecker, statistician for the Virginia Health Department and Mr. Louis Dunbar, statistician for the Metropolitan Life Insurance Company.

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THE DIAGNOSIS OF PEPTIC ULCER OF STOMACH AND DUODENUM.

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A peptic ulcer is an ulceration involving the mucous membranes of the stomach or duodenum. It is also known as a simple ulcer and is usually circumscribed and does not involve a wide area of the mucous membranes.

As to etiology, the literature contains little more than it did 35 years ago. There are several theories as to cause. It has been set forth that peptic ulcer may be produced by gastric fluid, local nutritional disturbance, embolism, endarteritis, traumatism, anemia, hyperchlorhydria, bacterial infection and toxic substances. The various causes are yet debatable and will, perhaps, remain so for sometime.

There is one striking feature about peptic ulcer patients, and that is, some focal infection can be demonstrated in the majority of cases coming under our observation. To further support this, we have repeatedly noted improvement in symptoms referable to peptic ulcer when the focus or foci of infection have been removed. We regard this more than a coincidence as we have known it to occur in fully 75 per cent of all cases observed.

The season of the year has, in some manner, some influence, as we have observed more ulcer cases for first time in spring and early fall. Further, cases that are under observation and not fully arrested or cured, tend to relapse during these two seasons. The relapsed cases usually respond very readily to treatment.

Another interesting point in our experience is the patient will occasionally give history of having had, at intervals, attacks of ulcerative stomatitis, which consisted of small punched out ulcers on mucous membranes, the borders of which have a grayish color with a crater like inflammation in center, comparable to peptic ulcer.

We are unable to make a satisfactory explanation as to the relation of stomatitis to peptic ulcer. This coincidence has caused us to regard the focal infection idea as causes of peptic ulcer more plausible. We do not know.

Peptic ulcer is more prevalent between the ages of 20 and 35. As to sex, men are more frequently affected.

Pathology: As to location, the pathologist says the posterior wall of the stomach along the lesser curvature near the pylorus is the most frequent area involved. If in duodenum, it is located usually in the first three inches beyond the pyloric ring.

The pathology will, obviously, be dependent upon the state of ulceration, whether acute or chronic. The peptic ulcer is usually solitary, but may be multiple, and if many are present they are usually grouped closely together. The ulcer may be saucer-shaped, terraced or funnel-shaped. The lesion involving the mucosa is nearly always large: there is less destruction of tissue when the muscular layer is involved. The margins may be sharp, punched out in appearance. The floor of the ulcer may be muscle or serous layers, or some adjacent viscus. In case of perforation the amount of secondary pathology may be little or widespread. The possibility of carcinoma being superimposed on the site of the peptic ulcer is to be kept constantly in mind.

Undoubtedly many ulcers occur and heal without producing alarming clinical symptoms.

The various deformities that peptic ulcer may produce is dependent upon the duration, severity, and location. The principal deformities consist of pyloric stenosis, hour-glass contraction, and other deformities with or without perforation.

Symptoms: This is debatable and one may ask, first, what constitutes an ulcer symptom? In other words, what is an ulcer history? An ulcer may exist, be found post-mortem, and no symptoms ante-mortem.

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The symptoms may be latent and only arise when there is perforation with associated peritonitis or fatal hemorrhage. Perforation may occur and produce no alarming symptoms, as has been revealed post-mortem—death being attributed to other causes, as acute infection.

We have had one patient in which his only symptom was that due to acute perforation while enjoying his midday meal. This ulcer was revealed three hours later by laparotomy. He states that he had no previous digestive disturbance: acute abdominal pain and shock were his warning of perforation. Therefore, it is not surprising that the profession cannot agree as to an all-enclosing "typical" history symptom-complex. Only can we classify an ulcer symptom when we regard the major symptoms as occur in those patients diagnosed ante-mortem or pre-operative. Therefore, the generally accepted ulcer symptoms are as follows:

1. *Pain.*—This may exist as an uneasy empty sensation to an acute agonizing paroxysm. Pain exists in about 90 per cent of all cases. It is most commonly located in epigastrium below the xiphoid cartilage, or 1 inch to the right of this area. This is dependent upon the location of ulcer. If to the right of the mid-line the pylorus or duodenum may be suspected. The pain is more commonly intermittent. It may be relieved or aggravated by food. The pain may occur at the height of digestion or two to four hours afterwards. When the pain is at its greatest intensity during the end of the digestion, an excess of hydrochloric acid may be suspected. In this event the taking of alkaline food, such as milk or albuminous food, will afford a certain amount of relief. Large amounts of heavy food frequently aggravate the pain. The pain is more frequently described as a "hunger pain." The patient forms a habit of taking some light food such as milk between his regular meals, also taking soda bicarbonate, or milk of magnesia, as this affords temporary relief. The pain may awaken him during the night, usually six to eight hours after his evening meal. Frequently the patient will have a glass of milk convenient to be taken during the night. The pain is usually a referred pain, a viscero-sensory reflex, and is not dependent on the organic changes in the gastric organ itself.

The characteristic feature about pain is its periodicity or regularity in which it occurs. Pain beginning one to three hours after meals, discontinuing one hour before next meal, suggests gastric ulcer. Pain beginning three to five hours after meals and continuing to next meal suggests duodenal ulcer.

2. *Loss of Weight and Strength.*—This we regard as next to pain in point of importance. We have seen cases in whom the outstanding symptoms were pain and loss of strength and weight. In spite of persistent inquiry these two symptoms were outstanding.

The patient will state he is eating more than ever, but in spite of this he continues to lose weight and strength. The loss of weight begins shortly after onset of pain in epigastrium. The weight loss is in proportion to the increasing frequency and severity of pain. It may be gradual, but each month or week there is some loss. There may be exceptions to this weight loss, but its prevalence is sufficient to list weight loss as a cardinal symptom. The weight may fluctuate, but in course of time a loss will be observed.

3. *Vomiting* may appear at weekly intervals, or it may be daily. It is usually preceded by pain. It may occur immediately after taking food or one to three hours later. The pain may be, and usually is, relieved by the act. The vomitus may consist of mucus, food, blood and highly acid fluid, depending upon time of occurrence with reference to time of taking food.

4. *Eructation* may occur immediately after taking food or during height of digestion. Frequently a sour or acid fluid is eructated, which produces a burning sensation in pharynx or substernal area, and is commonly referred to as "heart burn" or dyspepsia.

5. *Hematemesis*—or blood in vomitus—is the usual text-book symptom, but in our observation it is not frequent. Even in routine gastric analysis following Ewald meal, occult blood is rather rare. We are to keep in mind other causes for blood in vomitus, as the act of vomiting is a rather strenuous act. The effort may produce rupture of venules in the esophagus, pharynx or mouth, or from gingivitis and erosions. It is not advisable to depend upon the eye in studying vomitus, but chemical test should be made. When hematemesis is positive, it has considerable importance as an aid in making a diagnosis of gastric disease.

The test for occult blood is valuable only

after the patient has fasted for several hours, being careful to exclude other sources of blood, such as due to trauma or general systemic diseases. The quantity of blood may vary from a mere trace to a profuse and occasionally fatal hemorrhage. The symptoms will vary according to rapidity and amount of hemorrhage. The vomitus may be slight blood tinged, bright red to copious amount of coffee ground color, dependent upon frequency and amount of vomiting.

In acute ulcer the hemorrhage may be a spontaneous, alarming onset, without preceding history or symptoms. In chronic ulcer, the hemorrhage varies, while there is usually a history of chronic indigestion and a progressive anemia, and having previously vomited blood.

Blood when found in vomitus or in the stools, when other sources than peptic ulcer have been excluded, is a valuable aid in the diagnosis. Otherwise, it has no special significance.

With reference to symptoms, the essential factor is to develop the cardinal points in the history, for frequently the diagnosis can only be made in this way. Taken for granted that the symptoms are the so-called "typical of peptic ulcer," a diagnosis should never be undertaken without a thorough physical examination. In addition, the X-ray and laboratory study should be made in every patient, for the obvious reason that the diagnosis is arrived at by process of exclusion. Further, as previously stated in the etiology of peptic ulcer, focal infection is to be considered as a possible cause of peptic ulcer. The foci of infection, if present, should be recorded on the report.

Frequently the physical examination is negative. In fact, there are no outstanding signs produced by peptic ulcer. There is one sign that is present in a great majority—the presence of tenderness located in the mid-epigastrium. This is more common in gastric ulcer. If located one and one-half inches to the right of mid-epigastrium, it is more indicative of a pyloric or duodenal ulcer. No rule prevails as to referred sensory pain or tenderness to indicate which portion of stomach or duodenum is involved.

Occasionally deep palpation in this area will produce a dull aching sensation posteriorly at the angle of the left scapula. In atypical cases the tenderness may be diffuse, radiating in lesser intensity from the epigastrium. No tumor mass is ever palpable in acute ulcer. In chronic ulcer with considerable pathological change, much more may be found on examination, particularly should the patient be emaciated. In this event, gastro-enteroptosis may be expected and this is to be kept in mind with reference to location of the enclosed portion to be palpated. Should the ulceration be of long standing and symptoms of gastric stasis have been revealed, a dilatation of the stomach is to be expected.

Too much importance should not be given to the point of tenderness in epigastrium as at this point other conditions may be responsible by way of reflex.

X-ray examination is indispensable in properly studying these cases for peptic ulcer, and a final diagnosis should never be undertaken without its use. The examination should be made early in the morning before any food has been taken. This study should be made by a competent roentgenologist, as the shadows are not so evident that even "he who runs may read."

Final conclusions in the X-ray study should never be drawn until observed under the full physiological effects of atropin. This is especially important in acute ulcer and in nervous or excitable patients. Deformities, hypermotilities and muscular spasms will frequently disappear after the administration of atropin. Valuable information is made possible by a properly interpreted X-ray study.

Gastric analysis may show little. Whatever may be revealed, it is but one of the links in a chain leading to a diagnosis. The single test, or residue test as employed by some, we regard as a useless procedure, and fear it is used more for its psychological effect on the patient than for information obtained from the study of the gastric contents.

The fractional test is one of preference. The fasting residue should be withdrawn, after which an Ewald test-breakfast should be given; then specimens should be withdrawn every fifteen minutes for a period of two hours and laboratory study made. There are no typical findings, but here we have material to study.

A diagnosis of peptic ulcer cannot be made by gastric analysis. The acidity may, and usually does, vary from a low to very high acidity. Free hydrochloric acid may, in atypi-

XUM

cal and chronic cases, be absent. The presence of lactic acid is suggestive of stagnation from obstruction.

We do not permit the results of gastric analysis to influence us either way in arriving at our final conclusion, unless there is other corroborative evidence in our study.

Summary.

The final diagnosis is to be based on the following:

1. A careful and detailed history relating to digestive disturbances, as developed in symptoms of (a) pain in mid-epigastrium, varying in intensity from an uneasy feeling to sharp agonizing, boring pain, occurring at regular intervals, which may be relieved by taking of an alkali or some food, such as milk; (b) loss of weight and strength—gradual but progressive in proportion to other cardinal symptoms; (c) nausea and vomiting, usually associated with pain or taking of heavy foods, and this may occur immediately following a meal or during active digestion; (d) eructation, or so-called heartburn attacks; (e) hematemesis, or blood in the vomitus, varies in amount and frequency, but its presence may be important and significant.

2. Thorough physical examination, demonstrating usually an area of tenderness in mid-epigastrium. The presence of a focus or foci of infection likewise has to be borne in mind.

3. Fractional gastric analyses after an Ewald test meal, specimens to be obtained every fifteen minutes through a period of two hours.

4. Fluoroscopic and X-ray study before and after atropine medication.

TOXIN-ANTITOXIN.*

By J. A. NOBLIN, M. D., East Radford, Va.

Diphtheria today is known to be both curable and preventable. This seems almost incredible to many people, for only thirty years ago death claimed more than one-third of those attacked by the disease, and effective preventive means were unknown. This advance in medical knowledge stands as one of the major medical triumphs of all time.

For the protection of children there is a mixture known as toxin-antitoxin, which wide experience has proved to be effective in the prevention of diphtheria. Investigators found that by mixing diphtheria toxin with the right amount of antitoxin, the two neutralize each other so that the mixture is harmless. At the same time the toxin retains the capacity to stimulate the living body to produce its own antitoxin.

In 1913, after research workers had acquired considerable skill in the preparation and use of toxin-antitoxin, it was first used to immunize children against diphtheria.

The course of treatment is three doses of 1 c.c. each, given one week apart, and it requires two to six months before protection becomes complete. This protection lasts for years, perhaps for life.

By the use of a test devised by Dr. Schick, of Vienna, in 1913, we have a simple means of determining whether a person is susceptible to diphtheria. A very small amount of diphtheria toxin is injected into the skin: if the one tested is susceptible, the injection of the toxin will produce a slight local irritation, shown by a redness that develops in twenty-four to forty-eight hours. If not susceptible, no effect will be produced by the injection.

The use of this test has given us valuable information. It has shown that infants up to the age of six months are usually immune, and that children from nine months to six years are in the age group of highest susceptibility, and therefore in the greatest need of toxin-antitoxin.

In 1924 Dr. Giesen and myself gave it to our children. Early in 1925 I, as Health Officer, began to advocate strongly its use, and with the aid of the public health nurse, who urged its importance in the schools, and the endorsement of the State Board of Health, was able to induce twenty-five to take it.

In 1926, the superintendent of schools and the teachers became interested, and we got 122 to take the Schick test. These included teachers in all the grades and High School students, —persons from 40 years of age down. In this group we found sixty-one or exactly 50 per cent susceptible. This percentage would probably have been higher in small children. In 1927, 180 took it and, in the spring of 1928, 238 took it making a total of 580. This probably represents more than 90 per cent of all that have taken it in Radford. The number increases each year as parents come to know the importance of it.

We are urging all the younger school children to take it, and to bring their little brothers

*Read at the meeting of the Southwestern Virginia Medical Society in Wytheville, September 27-28, 1928.

and sisters for it, which many of them are beginning to do.

The clinics conducted by us in Radford and by the State in general have reached comparatively few children of pre-school age, as most of this work has been done in the schools. Our efforts must be concentrated more in immunizing the very young—from nine months to six years of age—as this is the group that most needs protection.

We have been able to get ninety-five of those who have taken toxin-antoxin back for the Schick test six months to two years after taking it, and have found only five who are not immune. We have not had a case of diphtheria in one who has taken the toxin-antitoxin, but we had a case in a young mother with a two year old child that had taken the toxin-antitoxin that did not contract it.

Whether diphtheria will ever cease to be a menace to childhood depends upon the readiness of the public, especially the parents of young children, to utilize the medical resources that are now available in the attack upon the disease. We have witnessed thirty-three years of progress in the fight against this grim enemy of little children. Medical science has discovered its cause, how it is transmitted, improved methods of diagnosis, a specific treatment, a test of susceptibility, and a sure and harmless method of prevention.

From the medical side, further improvements and refinements are to be expected, but with the practical knowledge already at our command, almost every case of diphtheria and every death therefrom is a direct challenge to our intelligence.

FIVE UNUSUAL CASES OF PERITONITIS.*

By THELMA F. BRUMFIELD, M. D., University, Va.
From Department of Pathology, University of Virginia.

Five recent cases of peritonitis are of interest because of their origins. They were well-distributed over the hospital services, one being medical, one surgical, one pediatric, and two urological. In no case was an antemortem diagnosis made which localized exactly the source of the peritonitis; and in three cases the existence of peritonitis was not diagnosed before autopsy.

The first was admitted on the Medical Service, and died a few hours later. A deep jaundice of three weeks' duration led to the suspicion of carcinoma at the head of the pancreas. At autopsy the peritoneal cavity was filled with thick greenish pus. The gall-bladder had completely sloughed away, and only a few fibrous remnants were left lying in a cavity of darker brownish pus and necrotic debris. The common duct was dilated to one centimeter in diameter, the wall was two millimeters thick, and it contained several faceted gall-stones. The liver was cirrhotic and showed multiple abscesses about the bile canals. The pancreas appeared normal on gross examination except for a slight fibrous thickening about the common duct. Microscopic study, however, showed small groups of cancer cells in the common duct and along the bile canals of the liver. The original growth may have occurred in the gall-bladder, and the peritonitis resulted from rupture here.

The second patient, a colored man, appeared to be improving for twelve days following a prostatectomy, when he suddenly complained of pain in the right upper quadrant. An exploratory laparotomy revealed an abdomen filled with pus and more concentrated about the lesser omentum, but no rupture in the stomach or appendix region was found. At the autopsy six days later, a cavity was felt opening at the bottom of the recto-vesical pouch. The prostatic bed appeared to be healing well, and it did not connect by any false channel with the cavity. Dissection of the region of the seminal vesicles showed the tubular tissue of the right one to be replaced by an abscess cavity, containing dark brown pus and debris, and opening into the peritoneal cavity. Also in the perineal region a thrombosed vessel was found and this was thought to be the source of pyemic infarcts in lung, spleen, kidney and intestine. Several facts make a diagnosis of the origin of the peritonitis in this case problematical. The first clinical symptoms occurred some time after the prostatic operation; they were of sudden onset and were located in the upper abdomen, suggesting a peritonitis of epigastric origin; it is possible that the rupture of the seminal vesical abscess into the peritoneum was an autopsy artefact, and was due to pressure exerted on a wall weakened by the abscess within. Widespread suppurative infarctions occurring in the spleen, the lung, and the lower loops of the ileum are possible sources of the peritonitis and would more readily fit the clinical pic-

*Read before the University of Virginia Medical Society.

ture of acute onset and the concentration of symptoms and pus in the upper abdomen. Nevertheless, the impression obtained by study of the autopsy was that peritonitis arose from rupture of the seminal vesical abscess.

The third case, an elderly colored woman, had suffered for several years from abdominal pain. Four days before death she was reported to have received a blow in the abdomen, but this she denied. She developed a sudden severe pain in the left lower quadrant and when admitted to the hospital her condition was too desperate to warrant operation. At autopsy the whole abdomen was found filled with a purulent exudate. A pyosalpinx on the left side, 5x3 cm. in size, showed a small rupture from which thick greenish pus was expressed. A few small cysts, 2x3 mm. in diameter, containing a clear fluid, were seen on the surface of this dilated tube, and the rupture occurred at the edge of one of these cysts. The right tube was congested, but showed no old adhesions and no evidence of a chronic pelvic inflammation.

Small cysts apparently similar to those found about the uterus and Fallopian tubes are described by Kaufmann as occurring in conditions of chronic salpingitis, and result from inflammatory hypertrophy of the glandular epithelium with its secondary cystic degeneration in the muscle wall. How much they contributed to the peritonitis, by causing a weakening of the tube wall, is a matter for conjecture.

Smears from the abdominal cavity and from the pyosalpinx appeared identical and were heavily loaded with a gram-positive diplococcus, apparently in pure form. Culture of the peritoneal pus showed the usual morphology and behavior of pneumococcus, and the organism was bile soluble. A broth culture from the pyosalpinx was taken later during the autopsy and handled by a student. It gave a heavy growth of bacillus coli, supposed to be a contamination.

The fourth case, an infant ten days old, died with signs of acute infection and increased intracranial pressure. The peritoneum was greatly congested and there was a thick yellowish mucoid exudate with occasional fibrinous clumps within the abdomen. The umbilicus appeared to be normally healed, but dissection of the right hypogastric artery revealed an unobliterated lumen filled with pus. The pelvic viscera were markedly congested. Smears showed streptococci, and the organisms could be seen lying in an abscess pocket in the microscopic tissues from the broad ligament. The meninges were also congested and showed streptococci in the exudate, while the skin was covered by a diffuse scarlatinal rash. No other focus for the infection was found except the umbilical vessels.

The last case, a white man, had suffered for years with kidney and ureteral stones. Six months before death the right kidney pelvis had been drained. At autopsy the peritoneal cavity contained quantities of thick pus more marked on the right side. The right kidney was smaller than the left, and it was adherent to the body wall and the colon. A peri-renal abscess, surrounded by a thick fibrous wall opened into the peritoneal cavity, and in this region there was thick inspissated pus. About an ounce of pus was drained from the kidney pelvis. The left kidney was also surrounded by abscess pockets, which were very thin-walled.

Kaufmann, in the last edition of his Special Pathological Anatomy, discusses the origin of peritonitis from various local suppurative processes. The origins of the four adult cases here reviewed are unusual, but not mentioned as being especially rare. The occurrence of a pneumococcus peritonitis originating in a Fallopian tube abscess in an elderly woman appears to be a distinct rarity, however, for over 75 per cent of pneumococcus peritonitis in a series of cases reported by Brunn (Da Costa's Modern Surgery) occurred in children, and it is especially apt to occur as a blood-borne infection secondary to a respiratory infection wth pneumococcus.

Fishbein reports twenty cases of peritonitis associated with salpingitis occurring in 184 postmortems on pertonitis, but the causative organisms are not individually reported and no case similar to the present was found discussed in the available literature.

Suppurative processes in the umbilical arteries resulting in peritonitis and generalized infection are discussed by Holt in his text-book on pediatrics, and they likewise are frequent enough to be considered as hazards in the first week of life.

In conclusion, five cases of peritonitis are presented, one originating through the rupture of a localized abscess in the gall-bladder region and associated with cancerous change, one from a pyosalpinx, one from the peri-renal tissues, and one of a questionable origin, probably from rupture of a seminal vesical abscess. The fifth case arose by extension from infection of the umbilical vessels. It is curious to note that contrary to our usual percentages, not one case of rupture of the gastro-intestinal tract has occurred in our series of autopsies this winter, and the only other case of general peritonitis resulted from an infected gunshot wound.

REFERENCE

Fishbein, Morris: A Contribution to the Bacteriology of Peritonitis, with Special Reference to Primary Peritonitis. *Am. J. Med. Sc.*, Vol. 144, p. 502. 1912.

PREGNANCY WITH COMPLICATIONS—CASE REPORTS—TUBERCULOSIS.

By
ALFRED N. BESSESEN, JR., M. D.,
and
DANIEL H. BESSESEN, M. D.,
Minneapolis, Minn.

Case 1. Mrs. F. N. L., seen first during June, 1923, at the age of 21, single, attending school. Had just had removed from under the left axilla lymph nodes which had been diagnosed tubercular microscopically. There was a clinical picture of active tuberculosis, with fever, anemia, loss of appetite and loss of weight. During the next year she received regular treatments from the mercury quartz lamp as an adjunct to sunlight, and in early August, 1924, a further diagnosis of intestinal tuberculosis was made following six or seven weeks of indigestion with febrile signs of active infection. She was placed in Glen Lake Sanatorium where, during a stay of three years, operation was performed to relieve symptoms of acute appendicitis, confirming the intestinal lesion—ileo-cecal. She was discharged from the sanatorium with arrested glandular tuberculosis and quiescent intestinal tuberculosis in January, 1927. In May of that year, she married and dated her first pregnancy from June 1, 1927. She was delivered from O. L. A. position at term, with second degree laceration. The placenta was delayed two and a half hours and was hastened by injection of 300 c.c. normal saline into the umbilical vein. One month following labor, the red count was 3,680,000, and haemoglobin 78 per cent. She was placed on high iron diet and rest, and convalesced satisfactorily with no indication of activation of either tuberculous lesion.

Case 2. Mrs. H. S., married, age 39, gravida 8, para 5, entered the clinic at nearly term with a past history of varicella, arthritis, pertussis, mumps. There was no abnormality noted in the family histories—marital, social, occupational or menstrual. She had had five children out of seven pregnancies, the third and sixth miscarrying at two and three months, respectively. Physical examination showed a badly infected mouth and a cystic goitre. At delivery there was an occipito-posterior presentation arrested in transverse. Version was performed and convalescence progressed with apparent normality. Nine months after delivery, the patient had fever, with cough, loss of appetite, loss of weight, severely infected teeth. Two sputa were examined and found negative for tubercle bacilli. The teeth were carefully extracted and the weight changed from 94 to 104 pounds in three months. In another thirty days, however, this weight was reduced to 100 pounds. At this time, fifteen months following labor, the patient developed erysipelas of the face, and from then on became rapidly worse, dying from far advanced pulmonary tuberculosis.

It is generally recognized that tuberculosis in other parts of the body is much less activated by pregnancy than is pulmonary tuberculosis. The time of greatest reaction is during the first trimester and during the months immediately following expulsion of the birth products.

In the first three months of pregnancy there is a slight weight loss (4 to 5 pounds) which is usually made up by the end of the third or fourth month. A rearrangement of the endocrine balance of the mother's body has become necessary and this reduces the nutrition of the patient slightly. Many patients develop vomiting, but all patients suffer a greater or less loss of weight. Loss of weight is the most commonly activating symptom of tuberculosis and is probably responsible for making the first trimester such a bugaboo for the tuberculous mother.

After this period, however, the mother customarily picks up in weight. There is an ability to utilize all food substance to its fullest

benefit. Unless the tuberculous lesion becomes active during the first three months, it is not likely to become so during the second or third trimesters.

An additional factor which brings this about is the anatomic change of the thorax during the last six months of pregnancy. The change is that of making the thorax more squat and broad, with shortening of the vertical measurement, and there is increase of the sagittal and horizontal measurements of the thoracic cavity. There is increase of the subcostal angle, and of the costo-vertebral angles, the ribs being lifted laterally, increasing the circumference of the chest and decreasing its expansion and excursion.

Immediately following labor, this anatomic change is completely rearranged, with a return of the lung shape to that preceding pregnancy. A transformation which has taken six to nine months to accomplish is reformed in four or five weeks. The effect is like suddenly removing a pneumothorax. Naturally, tuberculous lesions which exist in the lines of stress or pulling during this violent shaping of the lung tissue will be reopened, scar tissue is broken down, and activation results following labor. Some lesions, which may be active, may lie in situations of the thoracic cavity which allow the tissue to be put at rest by the change; while other cases present the opposite. The former are improved during gestation, while the latter are made worse. In both types of the condition, the violence of delivery may activate tuberculosis during the puerperium.

Further Zhurakovski has demonstrated by vital capacity experiments that the capacity of the lungs is increased 150 c.c. average by the ninth to twelfth day post-partum in 66.6 per cent of the cases. Recent studies on vital capacity in pregnancy show little or no changes during pregnancy, although change of this amount during parturition and early puerperium is sufficient to make extremely dangerous even a healed tuberculous lesion, let alone an active one.

5 *West Lake Street.*

Proceedings of Societies

The Post-Graduate Medical Society of Southern Virginia

Held its annual meeting at Waverly, Va., February the 12th, this being a most delightful and interesting occasion. There was a symposium on Influenza on which subject papers were read by Drs. J. Bolling Jones, W. A. Reese and Philip Jacbson, of Petersburg. This subject was freely discussed. The scientific meeting adjourned at six P. M. for supper, following which the nominating committee presented its report through its chairman, Dr. Wright Clarkson, of Petersburg. The following are the officers elected for the ensuing year: President, Dr. M. H. Tredway, Emporia; vice-presidents, Drs. F. N. Mallory, Lawrenceville, and W. W. Seward, Surry; secretary-treasurer, Dr. Philip Jacobson, Petersburg; chairman of Steering Committee, Dr. W. A. Reese, Petersburg. The Board of Censors is composed of Drs. T. F. Jarratt, Jarratt, H. G. Stoneham, Waverly, and Joel Crawford, Yale. The members of the Board of Public Health and Legislation are: Drs. J. Bolling Jones, Petersburg, W. M. Phipps, Hopewell, and L. O. Vaughan, Waverly.

The next meeting of this Society will be held at Emporia.

The Roanoke Academy of Medicine

Held a dinner meeting at the Elks Club, in Roanoke, Va., February the 18th. Following the dinner, a paper was presented by Dr. Thomas P. Sprunt, Associate in Clinical Medicine at Johns Hopkins University, his subject being "Classical Endocrine Syndromes with Remarks on Glandular Diagnosis and Organo-Therapy". This was illustrated with lantern slides.

The Danville Academy of Medicine,

At its regular meeting held in the dining room of Burton Hotel, that city, February the 12th, elected Dr. C. P. Howze, president; Dr. L. O. Crumpler vice-president; and Dr. J. J. Neal, secretary. Dr. I. C. Harrison and Dr. J. A. Hawkins are retiring president and secretary, respectively.

The University of Virginia Medical Society

Held its regular meeting on February 4, 1929, at 7:30, in the University of Virginia Hospital dining room. The meeting was called to order by Dr. Speidel.

Dr. Hopkins presented the first clinical case of Encephalitis in a young boy. Dr. Fletcher Woodward presented a case of Bronchiectasis which had been treated by tracheotomy with remarkable improvement. Dr. J. B. Graham reviewed two autopsy cases with demonstra-

tion of autopsy material from a case of Syphilitic Aortitis and from a case of Syphilitic Aneurysm of the ascending Aorta. The latter case was accompanied by an unusual lung finding in which the differential diagnosis of a widespread tuberculosis and fibrosis, and syphilitic fibrosis were discussed. Dr. W. W. Waddell, of the Pediatric Department, presented the main paper of the evening, "Feeding of Prematures", illustrated with slides. This paper has been published elsewhere.

The next regular meeting will be held February 18th, at 7:30 P. M.

At the meeting of this Society on February 18th, at the University Hospital, Dr. J. B. Graham demonstrated the pathological material from a case of pulmonary tuberculosis in which there was a complication of otitis media with mastoiditis.

Dr. E. C. Moore presented a case of lung suppuration following a tonsillectomy under general anaesthesia. Dr. Peterson exhibited a series of X-rays on the case. Dr. Graham showed the autopsy material from the case, particularly interesting tissue being the lung, showing the multiple abscesses.

Dr. W. H. Goodwin gave the main paper of the evening, *Bone Tumors*. He showed pictures of the cases, slides of the X-ray and the gross tissues of his series. Several interesting osteogenic sarcomas were exhibited, two of which have been entered in the Registry. (This paper will be published at an early date.)

Dr. C. B. Morton exhibited a patient with a rapidly growing osteogenic sarcoma of the upper end of the humerus. Dr. Peterson explained the X-ray findings in this case.

The next regular meeting will be held March 4th, at 7:30 P. M. All members of the Medical Society of Virginia are cordially invited to attend.

Woman's Auxiliary, Medical Society of Virginia

The Auxiliary's Task in Health Education.

The first request of the American Medical Association to the Woman's Auxiliary was that call to arms in educating the public in preventive medicine. To be able to do this work effectively the doctor's wives must first be educated themselves. Through living so close to the profession (wives naturally absorb knowledge from their husbands), they know the value of bodily health and proper living. It is easy for them to teach by their own example that wholesome living and frequent consultations with the family doctor will go much further toward maintaining good health then the treatment of disease.

The American Medical Association has also asked the Auxiliary to sponsor child health. What better work than this for the Woman's Auxiliary? Dr. Charles Mayo has said, "educate a child in health and you educate a whole family."

Health is now commonly listed as the first of the objectives of general education. Today the modern schools have health programs which are not limited to disease prevention, but to increase human happiness as well. This program aims at the attainment of health itself, not health knowledge merely. Leadership, active, informed, deliberate, should come from the doctor. The teacher and the public health nurse are the health teachers in the schools, the teacher as the regular health instructor and the nurse as the health advisor and assistant. The teacher must be a leader in school health, and must be equipped with knowledge and the art of healthful living herself. So health workers are concentrating on *teachers' training schools*, insisting that *allies not enemies* in the health crusade be graduated as teachers. The Auxiliary can be of great assistance in this work.

Even in schools where these programs are being carried on, the doctor's wives, as members of the Parent-Teacher's Association, can urge mothers to have children examined and all defects corrected before school begins.

National Chairman of Health Education for the Auxiliary, Mrs. George Hoxie, of Kansas City, asks that "the State and County Auxiliaries will keep in mind:

First—That personal hygiene, that is the principles upon which wise living must be based to make possible normal physical development and normal health, is necessarily dependent upon public hygiene.

Second—That since individuals and non-official organizations like ours cannot control public hygiene, every community must have official scientific health departments.

Third—That our first and most important

work is to secure such health departments, where they do not already exist; and

Fourth—Where they do exist that our most effective work can be done in co-operating with such official health departments to the end that they be made so effective as to be of the greatest possible good to the people they are maintained to serve."

Everything we do, therefore, from conducting baby clinics to showing health movies should be simply details of the ONE MAIN TASK.

ALICE LEIGH,
(MRS. SOUTHGATE LEIGH),
State Chairman of Health Education.

Auxiliary to the Norfolk County Medical Society

The executive board of this auxiliary had a tea on February the 9th at the home of its president, Mrs. M. N. King. The attendance was excellent and so enjoyable that it is thought this proves that more social life would help in attendance and interest of the various auxiliaries.

The Truth About Medicine

In addition to the articles enumerated in our letter of December 29th, the following have been accepted:

Ciba Company, Inc.
Lipoiodine—Ciba, Diagnostic.
Ampules Lipoiodine—Ciba, Diagnostic, 5 c.c.

H. K. Mulford Co.
Acidophilus Bacillus Liquid—Mulford.

E. R. Squibb & Sons
Dandelion Pollen Allergen Solution—Squibb; English.
Plantain Pollen Allergen Solution—Squibb; Goldenrod.
Pollen Allergen Solution—Squibb; Perennial Rye Grass.
Pollen Allergen Solution—Squibb; Ragweed (Dwarf).
Pollen Allergen Solution—Squibb; Ragweed (Giant).
Pollen Allergen Solution—Squibb; Red Top Pollen.
Allergen Solution—Squibb; Russian Thistle Pollen.
Allergen Solution—Squibb; Sunflower Pollen Allergen.
Solution—Squibb; Bermuda Grass Pollen Allergen Solution—Squibb, 5 c.c.; June Grass Pollen Allergen Solution—Squibb, 5 c.c.; Mugwort Pollen Allergen Solution—Squibb, 5 c.c.; Orchard Grass Pollen Allergen Solution—Squibb, 5 c.c.; Sagebrush Pollen Allergen Solution—Squibb, 5 c.c.; Western Ragweed Pollen Allergen Solution—Squibb, 5 c.c.

NEW AND NON-OFFICIAL REMEDIES

Normal Horse Serum.—A normal horse serum (New and Non-official Remedies, 1928, p. 348), marketed in packages of one syringe containing 10 c.c.; in packages of two syringes each containing 10 c.c.; in packages of one vial containing 25 c.c.; in packages of one double ended vial containing 50 c.c.; also in packages of one double ended vial containing 100 c.c. (The National Drug Co., Philadelphia).

Diphtheria Antitoxin, Extra Concentrated.—A diphtheria antitoxin, concentrated (New and Non-official Remedies, 1928, p. 352), prepared by inoculating horses with diphtheria toxin. It is marketed in single vial packages of 1,000 and 20,000 units; in syringes containing, respectively, 1,000, 3,000, 5,000, 10,000 and 20,000 units. (The National Drug Co., Philadelphia).

Tetanus Antitoxin.—A tetanus antitoxin, concentrated (New and Non-official Remedies, 1928, p. 356), prepared by inoculating horses with tetanus toxin. It is marketed in packages of one vial containing 1,500 units; in packages of one syringe containing 1,500 units; also in packages of one syringe containing 5,000 units. (The National Drug Co., Philadelphia).

Antistreptococcic Serum.—A polyvalent antistreptococcus serum (New and Non-official Remedies, 1928, p. 361), obtained by immunizing horses with streptococci from various clinical sources. It is marketed in packages of one syringe containing 20 c.c. and in packages of one double ended vial containing 50 c.c. (The National Drug Co., Philadelphia).

Vaccine Virus.—A vaccine virus (New and Non-official Remedies, 1928, p. 362), marketed in packages containing, respectively, one, five and ten capillary tubes. (The National Drug Co., Philadelphia).

Rabies Vaccine—Human (Semple Method).—An antirabic vaccine (New and Non-official Remedies, 1928, p. 363), prepared according to the general method of David Semple (phenol killed). Marketed in sets of two packages, the first containing four 2 c.c. vials and the second containing ten 2 c.c. vials. (The National Drug Co., Philadelphia).

Pertussis Vaccine.—A pertussis bacillus vaccine (New and Non-official Remedies, 1928, p. 376), marketed in packages of one 5 c.c. vial containing 4,000 million killed pertussis bacilli per c.c.; in packages of one 15 c.c. vial containing 4,000 million killed pertussis bacilli per c.c.; in packages of one 30 c.c. vial containing 4,000 million killed pertussis bacilli per c.c. (The National Drug Co., Philadelphia).

Pneumococcus Vaccine.—A pneumococcus vaccine (New and Non-official Remedies, 1928, p. 379), marketed in packages of one 5 c.c. vial containing 5,000 million killed pneumococci per c.c.; in packages of one 15 c.c. vial containing 5,000 million killed pneumococci per c.c.; in packages of one 30 c.c. vial containing 5,000 million killed pneumococci per c.c. (The National Drug Co., Philadelphia).

Staphylococcus Vaccine.—A staphylococcus vaccine (New and Non-official Remedies, 1928, p. 391), marketed in packages of one 5 c.c. vial containing 2,000 million killed bacilli per c.c.; in packages of one 15 c.c. vial containing 2,000 million killed bacilli per c.c.; in packages of one 30 c.c. vial containing 2,000 million killed bacilli per c.c. (The National Drug Co., Philadelphia).

Typhoid Vaccine.—A typhoid vaccine (New and Non-official Remedies, 1928, p. 383), marketed in packages of one 5 c.c. vial containing 1,500 million killed typhoid bacilli per c.c.; in packages of one 15 c.c. vial containing 1,500 million killed typhoid bacilli per c.c.; in packages of one 30 c.c. vial containing 1,500 million killed typhoid bacilli per c.c. (The National Drug Co., Philadelphia).

Typhoid-Paratyphoid Combined Vaccine.—A typhoid vaccine (New and Non-official Remedies, 1928, p. 383), marketed in packages of three 1 c c. vials, the first dose containing 500 million killed typhoid bacilli, 375 million killed paratyphoid A bacilli and 375 million killed paratyphoid B bacilli, the second and third doses each containing 1,000 million killed typhoid bacilli, 750 million killed paratyphoid A bacilli and 750 million killed paratyphoid B bacilli; in packages of one 5 c.c. vial containing 1,000 million killed typhoid bacilli, 750 million killed paratyphoid A bacilli and 750 million killed paratyphoid B bacilli per c.c.; in packages of one 15 c.c. vial containing 1,000 million killed typhoid bacilli, 750 million killed paratyphoid A bacilli and 750 million killed paratyphoid B bacilli per c.c.; in packages of one 30 c.c. vial containing 1,000 million killed typhoid bacilli, 750 million killed paratyphoid A bacilli and 750 million killed paratyphoid B bacalli per c.c.; in packages of ninety 1 c c. vials (thirty immunizations), being thirty sets of three doses, the first dose containing 500 million killed typhoid bacilli and 375 million each of killed paratyphoid A and B bacilli, the second and third doses containing, respectively, twice the number of bacilli in the first dose. (The National Drug Co, Philadelphia).

Typhoid-Paratyphoid A Vaccine.—A typhoid vaccine (New and Non-official Remedies, 1928, p. 383), marketed in packages of one 5 c.c. vial containing 750 million killed typhoid bacilli and 250 million killed paratyphoid A bacilli per c.c.; in packages of one 15 c.c. vial containing 750 million killed typhoid bacilli and 250 million killed paratyphoid A bacilli per c.c.; in packages of one 30 c.c. vial containing 750 million killed typhoid bacilli and 250 million killed paratyphoid A bacilli per c.c. (The National Drug Co., Philadelphia).

Scarlet Fever Streptococcus Toxin for Preventive Immunization—P. D. & Co.—It is prepared by the method of Drs. Dick, by license of the Scarlet Fever Committee, Inc. (New and Non-official Remedies, 1928, p. 392). Marketed in packages of five vials of toxin, containing, respectively, 500, 2,000, 8,000, 25,000 and 80,000 skin test doses; in packages of fifty vials of toxin, ten containing 500 skin test doses, ten containing 2,000 skin test doses, ten containing 8,000 skin test doses, ten containing 25,000 skin test doses, and ten containing 80.000 skin test doses. Parke, Davis & Co., Detroit. (Jour. A. M. A., January 5, 1929, p. 55).

Bothrops Antitoxin.—An antitoxic serum prepared by immunizing animals against the venom of the tropical American serpents of the genus *Bothrops*. Evidence has accumulated to show that the venom of certain snakes may be neutralized by the employment of a serum obtained from animals that have been injected with venom from a snake of the same family. Bothrops antitoxin is used to neutralize the venom injected by the bite inflicted by members of the genus *Bothrops*. The serum is administered intramuscularly or subcutaneously; in cases seen late or in the presence of severe symptoms it may be administered intravenously.

Antivenin (Bothropic).—Tropical American Anti-Snake-Bite Serum—An antitoxic serum prepared by injecting horses with venom from serpents of the genus *Bothrops*, especially of the "Fer-de-Lance" (*Bothrops atrox*). It is claimed to have neturalizing effect against the venom of the genus represented. The serum is marketed in syringes of 10 c.c. (a single dose). H. K. Mulford Co., Philadelphia.

Ephedrine Hydrochloride—Lilly.—A brand of ephedrine hydrochloride.—N. N. R. (New and Non-official Remedies, 1928, p. 175). It is also supplied in the form of Pulvules Ephedrine Hydrochloride—Lilly, ⅜ grain, Pulvules Ephedrine Hydrochloride—Lilly, ¾ grain and Solution Ephedrine Hydrochloride—Lilly, 3%. Eli Lilly & Co., Indianapolis.

Tablets Ephedrine Hydrochloride—Squibb, ⅜ grain.—Each tablet contains ephedrine hydrochloride—Squibb (*The Journal*, September 1, 1928, p. 645), ⅜ grain. E. R. Squibb & Sons, New York.

Book Announcements

Vocabulary of the Kiowa Language. By JOHN P. HARRINGTON. United States Government Printing Office, Washington. 1928. Smithsonian Institution, Bureau of American Ethnology, Bulletin 84. Octavo of 255 pages. Cloth.

Textbook of Clinical Neurology, for Students and Practitioners. By M. NEUSTAEDTER, M. D., Ph. D., Visiting Neurologist, Central Neurological Hospital, Welfare Island; Clinical Professor in Neurology, New York Polyclinic Medical School and Hospital, etc. With an **Introduction** by EDWARD D. FISHER, M. D., Professor Emeritus of Neurology, University and Bellevue Hospital Medical College, New York. Philadelphia. F. A. Davis Company, Publishers. 1929. Octavo of 602 pages with 228 illustrations, some in colors. Cloth. Price, $6.00 net.

Spinal Anesthesia (Subarachnoid Radicular Conduction Block) **Principles and Technique.** By CHARLES H. EVANS, M. D., Clinical Assistant, N. Y. Post-Graduate Medical School and Hospital, Lying-In Hospital of the City of New York, etc. **Introduction** by W. WAYNE BABCOCK, M. D., F. A. C. S. **Foreword** by CHARLES GORDON HEYD, M. D., F. A. C. S. Octavo of 203 pages with 41 illustrations, 3 in color and 1 folding colored plate. Paul B. Hoeber, Inc. New York. 1929. Cloth. Price, $5.50 net.

Angina Pectoris. By HARLOW BROOKS, M. D., Emeritus Professor of Clinical Medicine, New York University; Visiting Physician, City Hospital, etc. **Harper's Medical Monographs.** Harper & Brothers. New York and London. 1929. 12mo. of 164 pages. Leatherette. Price, $2.50.

The National Health Series. Diabetes and Its Treatment. By FREDERICK M. ALLEN, M. D., Director of the Physiatric Institute, Morristown, N. J. **What Every One Should Know About Eyes.** By F. PARK LEWIS, M. D., F. A. C. S., Vice-President, National Society for the Prevention of Blindness. **Care of the Mouth and Teeth.** By HARVEY J. BURKHART, D. D. S., LL. D., Director, Rochester Dental Dispensary, Rochester, N. Y. Edited by THE NATIONAL HEALTH COUNCIL. Funk and Wagnalls. New York and London. 1928. Leatherette. Pocket size. Price, 30 cents each.

Certified Milk Conferences held in 1928. Annual Conference **American Association of Medical Milk Commissions, Inc.,** and **Certified Milk Producers' Association of America, Inc.,** Minneapolis, Minn., June 11-12, 1928. Annual Conference **Metropolitan Certified Milk Producers, Inc.,** with the **Certified Milk Producers' Association of America, Inc.,** New York, N. Y., February 6, 1928, etc.

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Editorial

Carcinoma of the Pancreas.

Based upon a study of 37 cases and presenting observations from a reference literature of wide range, a paper of Friedenwald and Cullen* is taken as a convenient source for editorial comment here. Perusal of the paper gives one an opportunity for refreshing one's mind on the subject.

The symptomatology may be quite indefinite in the early stages of the disease. There may be only mild digestive discomfort, such as one may hear from any "dyspeptic", eructations, nausea, and loss of appetite. Later, as the disease progresses, pain, malaise, vomiting, and gradually deepening jaundice, loss of flesh, and cachexia appear. Fever eventually appears. Patients in the fifth decade, presenting such symptoms, may be strongly suspected of having malignant disease of the pancreas.

Digestive disturbance such as pain, described as a feeling of fullness and pressure, becoming more and more intense, possibly colicky in type, mark the appearance of grave involvement of the pancreas. Eusterman observed that 88 per cent of cases complain of pain. Nausea and vomiting were found in 33 out of 37 of the author's cases, while pain occurred in 31 out of 37 cases. Tenderness on pressure in the epigastrium and at times under the right costal border is frequent. Jaundice due to obstruction of the common duct was found in 26 out of the 37 cases. Absence of free hydrochloric acid was noted as common. Diarrhea and constipation, alternating, are commonly present. Fat and undigested muscle fiber in stools of a bulky nature were found.

*The American Journal of the Medical Sciences, July, 1928.

Tumor mass and enlargement of the gall-bladder are outstanding and important signs. In this connection, enlargement of the liver is found; at least 40 per cent of cases show this association. The gall-bladder is distended; when demonstrable, it is a real diagnostic sign. In Futcher's report 70 per cent showed the gall-bladder distention. The authors point out the observation that in Ecklin's report of 172 cases of obstruction of the common duct due to gall-stones, the gall-bladder was contracted in 70 per cent, while in 61 cases of carcinoma of the pancreas, gall-bladder was dilated in 96 per cent. Tumor mass, according to Futcher's and Kiefer's figures, may be palpated in 39 per cent to 30 per cent of cases, while the authors' figures give 43 per cent, they having been able to make out tumor mass in 16 cases.

Outstanding symptoms arising from involvement of the pancreas, but shown through pressure effects and causes are worthy of comment. Cancer of the pancreas rarely causes diabetes, but transient glycosuria, sometimes permanent, is found in these cases. About 10 per cent show transient glycosuria. The authors' cases showed transient glycosuria in 6 per cent. Bile is present in urine in all jaundiced cases. Ascites and edema of the extremities are found in later stages of the disease and when the pressure is made upon the portal vein, vena cava, or by secondary involvement of the liver, adjacent.

Obstructive symptoms occur. Pressure upon the pylorus or duodenum may produce ugly gastric symptoms; obstruction of the intestines and enlargement of the spleen may throw in a complicating group of symptoms in some cases. In the matter of diagnosis, the authors of the paper, under comment, take the reasonable position that diagnosis of cancer of the pancreas "can be made with ease in about one-half of the cases; 'other cases may be' extremely difficult." It is easy to make the diagnosis in patients who give a history of indigestion, increasing pain in the upper abdomen, deep jaundice, rapid emaciation, and cachexia. But in the incipient stages with an absence of several of the symptoms, as may occur, the accuracy of the diagnosis is more uncertain. Physicians must be on the alert for that case of cancer of the pancreas that presents symptoms of digestive disturbance of the stomach associated with recurrence of persistent diarrhea. In the patient past middle life who

shows gastric disturbance, pain in the epigastrium, fatty diarrhea, with a marked anemia, one may think strongly of cancer of the pancrease, as one endeavors to arrive at a differential diagnosis. Because, among a group of conditions, such as chronic pancreatic cholelithiasis, or cholecystitis, cancer of the liver or gall-bladder, one has to make a careful differentiaton in an assembly of symptoms much alike.

Primary Carcinoma of the Lung.

In touching upon this subject, the idea that it is a rare condition must be given up. Carcinoma is on the increase in America and abroad, and primary carcinoma of the lung is found at autopsy once in every 200 deaths from carcinoma, and is found once in every 200 autopsies upon adults. So it is not improbable that the idea of the rarity of the disease has been estimated by the failure in recognizing it in pulmonary cases in the fifth, sixth, and seventh decades of life.

It is probably wise for our readers to consider anew, if only in such a sketchy manner, certain leading or cardinal symptoms and signs. The list of symptoms of the disease may be wanting in any real individuality. There may be cough, pain in the chest, a certain sort of sputum, dyspnea, cyanosis, dysphagia, stertor, and effusion. In case of carcinoma of the mediastinum, there may be cough, pain in the chest, dyspnea, cyanosis, venous engorgement and edema of the upper part of the body, paralysis of the recurrent laryngeal nerve, hoarseness, inequality of the pupils, abdominal pain, dysphagia, and stertor. Certain general systemic signs are associated with this such as loss of weight, weakness, osteoarthropathy, fever, chills, and anorexia. Further, association of symptoms due to metastasis may be noted as found in evidence of the involvement of the central nervous system, pain in the lower extremities, pain in the back, and abdominal pain. The findings of physical examination necessarily vary over a wide range. The stage and state of progress and complicating factors bring a varied assortment of signs by inspection, palpation, percussion and auscultation. The area of dullness, increasing progressively, marks the neoplastic mass in the more advanced cases. Naturally, lung parenchyma may emit signs that vary.

Weller's twelve cases form an interesting story in the description of primary carcinoma of the lung and can be read by practitioners with profit. Case one, presenting symptoms of coma, cyanosis and dyspnea, gave a pathologic diagnosis of stenosis, primary adeno-carcinoma of the right main bronchus, metastasis in bronchial lymph nodes and left kidney, acute stenosis of the trachea, partial stricture of the esophagus, chronic purulent fibroid pneumonia, bronchiectasis, emphysema, chronic leptomeningitis, atrophy with acute and chronic passive congestion of all organs. Case two displayed abdominal pain and much difficulty was experienced in arriving at a correct diagnosis. X-ray of the chest disclosed increased density of the hilum and other foci. Case three displayed vomiting, abdominal pain, and loss of weight. In case four pain in the legs dominated the picture. In case five, engorgement of the superficial veins and hoarseness were the most striking signs. Case six showed mainly enlarged cervical nodes and weakness. Case seven complained of pain in the arms and chest, hoarseness, and showed pupillary inequality. Case eight gave a history of pain in the back and showed paralysis of the lower extremities. Case nine complained of pain in the feet and legs and was confused with aortic aneurism. Case ten gave out the following chief signs—cough, hemoptysis, dyspnea, fever and empyema. Case eleven complained of pain in the chest, productive cough, and weakness. Case twelve gave a clinical history chiefly of pain in legs. A rich array of symptoms and signs may be found as one peruses the interesting case reports, autopsy reports, and the records of the pathological diagnosis. To follow carefully this excellent presentation of the subject is to renew one's knowledge of the physical findings of these cases. Weller's paper should be read with interest.

Reference: Annals of Internal Medicine, February, 1929.

Tumors and Inflammations of the Mediastinum.

An anatomical description, even in brief, is quite necessary in this comment. This space, between the approximate reflections of the pleurae in the median line, contains three general compartments. In the anterior mediastinum, there were found loose areolar tissues, lymphatic vessels, the remains of the thymus gland, the internal mammary vessels of the left side, and the origin of sternohyoid, sternothyroid, and the triangularis muscles. The middle mediastinum holds within its confines

the heart in its pericardium, the ascending aorta, the super vena cava, the bifurcation of the trachea, the pulmonary arteries and veins, and the phrenic nerve. The posterior, lying between the posterior part of the pericardium and the vertebral line, holds the descending aorta, the greater and less azygos veins, the esophagus, the pneumogastric nerves and the great splanchnic nerves.

This middle septum between the two lungs, within the thorax, as one may easily conceive, may cover the site of serious inflammatory and chronic pathology. The proximity of this closed space to the great arterial and venous vessels of the body, the close contact of this compartment with its lymphatic and nerve lines, with the inflammation of the heart and pericardium, the ultimate relation of the visceral stock of the mediastinal chamber with the inflammation of the larynx, trachea and bronchi, the rich and abundant converging of the lymphatic system, with its frequent inflammatory and pathologic enlargements, all make for the easy possibility of the occurrence of acute inflammatory phenomena and, also, with tuberculosis, syphilis, and cancer, as a triumvirate of not infrequent focal occurrence within this general area of the body, of chronic pathologic growths.

Inflammatory changes of the mediastinum are roughly found to fall under the general terms of lymphadenitis, acute mediastinitis and chronic mediastinitis, while tumor growths of the mediastinum are sarcoma and lymphosarcoma, carcinoma, endothelioma, thyroid tumors, enlarged lymph nodes and cysts.

With these general facts in mind, practitioners, who are daily in touch with patients past middle life suffering with diseases affecting the organs of respiration and the heart, and who have primary evidence of syphilis and tuberculosis, may recall some of the symptoms and physical signs emanating from pressure signs of the mediastinum.

Fortunately or unfortunately, according to the view one takes, the mediastinum may be the site of inflammation and chronic growth of no small degree and yet "kick-up" no serious or distressing symptoms or signs. It may be easily understood that infected lymph nodes and other inflammatory processes may follow acute infections of the pleura, lungs, pericaridum, trachea, and other organs adjacent, and yet not bring the patient to the physician.

It is usually after growth and pressure symptoms exhibit distressing proportions of dyspnea, cough, pain and circulatory disturbances that mediastinal disorders are presented by patients for diagnosis. As these symptoms are present in other very important disease-conditions within the chest, it becomes a matter of importance to interpret them.

Dyspnea, with constriction and oppression in the chest, cough, paroxymsmal in character accompanied by stridor, pain within the chest, associated with respiratory disturbances like laryngeal paralysis or asthma phenomena, circulatory disturbance of heart as bradycardia or tachycardia, disturbance of diaphragm and other assortment of symptoms, directs one's mind to the pressure effects of a tumor of the viscera of the mediastinal space within the anterior, middle or posterior division or a combination of all.

Physical signs here are signs of late changes. Bulging of the chest, fullness of intercostal spaces, displacement forward of the sternum, enlargement of the lymphatics of the neck, signs of difficult breathing, pulsations and distended vessels may be gotten on inspection. Percussion over the chest with aggravated signs as mentioned above gives dullness or flatness over the growth within.

Signs of venous congestion and edema stand out as evidences of pressure. Until the collateral circulation becomes established, these signs may be extremely annoying. In this as in all chest pathology, X-ray examinations materially aid the examiner. While it is relatively easy to determine the pressure of a mass in the mediastinum, it is not at all easy to determine the nature of the tumor. In addition it is not easy to differentiate between tumors of the anterior and posterior mediastinum.

Reference: Oxford Medicine II, Chapter VI.

Chronic Mediastinitis.

This condition is often overlooked. There may be a group of inflammatory processes of varying origin in the structure of the mediastinum. The fact remains that no matter what the etiologic nature of the process is, the thickening and increase of connective tissues occurs and when these processes reach proportions sufficient to produce pressure effects, symptoms present themselves—at first not very characteristic but later pointing more directly to the mediastinum. There are three general causes: (1) Syphilis that may symptomatically be mild in the earlier stage; (2) tuberculosis, that is usually of the lymph nodes, sometimes bone

structure; and (3) other infections associated with infections of the nose, throat, lungs, and pericardium.

Symptoms of the condition depend upon the nature, location and degree of the inflammatory processes. Obstructive symptoms of venous circulation present signs of importance in mediastinitis. Dyspnea on effort and venous obstruction signs make one thing of the mediastinum. Following or associated with these are cyanosis and oppression. Later, cyanosis becomes fixed and emphatic and edema occurs The gross changes of the upper chest and face later present bloated and swollen features of a bluish red color. Eyes take on prominence. The venous tortuosity and dilatation become extremely exaggerated.

The physical signs vary and the diagnosis will rest upon the history, symptoms, physical findings, laboratory examinations and X-ray study.

Council Approves Sheppard-Towner Act.

The Council of the Medical Society of Virginia at its meeting on February 26, 1929, approved a continuance of the Sheppard-Towner Act.

Virtually half of Virginia's counties now have nursing services that are being aided by contributions from the joint maternity and infancy fund to which the State and the Federal Government are equal contributors. The Federal Government really gives more money since it appropriates to each State $5,000 of unmatched funds which is supposed to be sufficient for all overhead expenses of administering this fund.

In Virginia, no Sheppard-Towner program has been inaugurated until it had been approved by the authorized representatives of the Medical Society of Virginia; and there has been no variation from any program without the consent and approval of such representatives. Therefore, it was to have been anticipated that the Council of the Society would view, without sympathy, efforts which are being made to have it appear that the Sheppard-Towner work is disapproved by the medical profession generally.

Nevertheless, it is peculiarly gratifying to the public health authorities of the State that the Council showed the wisdom and farsightedness to place itself on record as approving the activities conducted under the Sheppard-Towner Act and, by inference, supporting those who are now asking that this Act be continued. And it will be peculiarly gratifying to the poor mothers in far remote rural sections who will understand from such action that the great medical profession sympathizes with them and wishes to do all in its power to make their troubles lighter and their dangers less.

Intelligent selfishness, to put the matter on no higher ground, should incline doctors to favor this measure. Among the outstanding accomplishments of the Sheppard-Towner work in Virginia has been the material reduction in the number of ignorant midwives and the considerable instruction of the better ones to recognize before it is too late cases which require medical attention. Unfortunately, the distribution of doctors in our rural sections makes it extremely difficult for rural mothers to obtain medical care at the time of childbirth; but by the training of the more intelligent midwives and the holding of institutes for doctors' helpers together with the printed lessons to mothers and prospective mothers—all efforts made possible by Sheppard-Towner aid—the pathologic cases will be more sure of attention even if the physiologic cases cannot secure medical care.

In this respect, Virginia has no greater difficulties than have other States. The scarcity of doctors in rural sections is a national problem. It is, indeed, a pity that city physicians in certain sections of the country uninformed as to the problems of the sparsely settled areas, are trying with some success to becloud the issue; but on the other hand it is fine to know that they are not succeeding in Virginia.

News Notes

Health Workers Hold Annual Meeting.

The annual conference of state health workers conjointly with the Virginia Public Health Association was held in Richmond on February 18th, 19th, 20th, and 21st. Most of the county health officers, public health nurses, sanitation men and many city health officers with their staffs were in attendance. General meetings were held in the community house of the Broad Street Methodist Church and sectional meetings were held at Cabaniss Hall, Medical College of Virginia and at the State Health Department.

Distinguished out of State visitors were present and participated in the discussions. Dr. W. F. Draper, Assistant Surgeon Gen-

XUM

eral of the U. S. Public Health Service, Dr. John A. Ferrell, Director for the United States for the Rockefeller Foundation, Miss Elizabeth Fox, Director of Public Health Nurses, American Red Cross, Dr. Nathan Sinai, Director National Committee on the Cost of Medical Care of the American Medical Association, and Dr. W. W. Cort, Professor in Johns Hopkins School of Hygiene and Public Health, were among these.

The first session of the conference was given over to an exhaustive discussion of Dr. M. E. Brydon's plan to sanitate Virginia in the next three years. This plan contemplates the enlistment of the housekeepers of the State in a concerted organized effort to provide the details of safe sewage disposal, safe water, screens and fly control at each home in the State. Substantial money prizes are offered to the organization in the counties that achieve the best results under this plan. Dr. Brydon, Dr. Ennion Williams and Col. Kelley explained the plan and answered the many questions submitted by the audience.

The address by Miss Fox on the Red Cross in action during the hurricane disasters in Porto Rico and Florida was most interesting. Her statement that on reports from the weather bureau the Florida disaster was anticipated and workers dispatched to the scene and warnings given twenty-four hours ahead of the storm was especially striking.

Dr. Nathan Sinai, Director of the National Committee on Cost of Medical Care, addressed the conference on his researches in this field. Mr. Frank Bane, State Welfare Commissioner of Virginia, gave an address on the recently organized psychiatric clinic work in Virginia.

Dr. C. B. Ransome, Health Officer of Roanoke, President of the Virginia Public Health Association, took as the subject of his presidential address "Syphilis the Greatest Killing Disease" and by a large statistical chart made out a very strong case against this disease.

Dr. L. T. Royster, Professor of Pediatrics, University of Virginia, gave an address on "Mortality in Infancy and Childhood" which was filled with apt and valuable suggestions to workers in the maternity and infancy field.

Dr. W. W. Cort, Professor in the School of Public Health and Hygiene, Johns Hopkins University, discussed the role ascaris plays in the morbidity among children and described the methods and results of his recent ascaris survey in Wise County, Va.

Dr. L. J. Roper, City Health Officer, Portsmouth, Va., discussed morbidity reports. Dr. W. B Foster, City Health Officer, of Richmond, addressed the meeting on health department clinics. Dr. W. A. Plecker, Director Bureau Vital Statistics, gave an interesting paper on "Rheumatism a Public Health Problem" and Dr. L. L. Williams, Surgeon, U. S. Public Health Service, showed a most instructive moving picture on malaria control. Dr. W. A. Bmrufield, Director of the Nine-County health unit centering around Farmville, described his work and what he hoped to accomplish.

Section meetings of the Tuberculosis Bureau, of the public health nurses and of the health and sanitation officers which discussed in detail the peculiar problems in the separate fields were most productive of fruitful suggestions. Dr. Dean Cole gave a lecture illustrated by a moving picture reel on "Differential Diagnosis of Early Tuberculosis". Mr. Berry, Director of Shellfish Sanitation for Virginia, presented a model ordinance for cities and towns in the control of the sanitary distribution of oysters and other shellfish. Dr. Harvey Coghill discussed practical child psychology and State Health Department staff and field workers dealt with the important details of their work.

Prizes were awarded nurses and sanitation officers for the best essays on subjects in their separate fields.

The Virginia Public Health Association elected as its officers for the ensuing year the following: President, Dr. W. Brownley Foster, Richmond; Vice-Presidents, Dr. W. H. Pott, Portsmouth and Dr. G. F. McGinnes, Richmond; Secretary-Treasurer, Dr. F. J. Wampler, Richmond.

Dr. Mosby G. Perrow, Director Public Welfare, Lynchburg, was elected as representative of the Association to the American Public Health Association.

The Tri-State Medical Association of the Carolinas and Virginia

Held a most interesting and pleasant session in Greensboro, N. C., in February, under the presidency of Dr. James K. Hall, of Richmond. Interesting clinics added much to the value of this meeting. Charleston, S. C., was selected as the 1930 place of meeting, and

the following officers were electd for the coming year: President, Dr. Cyrus Thompson, Jacksonville, N. C.; vice-presidents, Dr. W. R. Wallace, Chester, S. C., Dr. J. M. Baker, Tarboro, N. C., and Dr. Frank S. Johns, Richmond, Va. Dr. J. M. Northington, Charlotte, N. C., was unanimously re-elected secretary-treasurer and was at the same time voted an appreciation of the work he had done in this capacity and also as editor of *Southern Medicine and Surgery.*

The Virginia Tuberculosis Association

Held its annual meeting in Richmond on February the 28th. In addition to an interesting program by members, Dr. Kendall Emerson, New York, mangaging director of the National Tuberculosis Association, talked at the morning session on "Local Tuberculosis Programs". In the evening he delivered an address to the profession and the public.

At the business meeting Dr. Dean B. Cole, Richmond, was elected president of the Association for the ensuing year; Dr. H. A. Latane, Alexandria, was elected first vice-president, and Dr. Roy K. Flannagan, Richmond, secretary. Miss Leslie Combs Foster was re-elected executive secretary-treasurer.

Dates Set for State Society Meeting.

The Council held its mid-winter meeting on February the 26th, at which time October 22nd, 23rd and 24th were selected at dates for our annual meeting in Charlottesville, Va., under the presidency of Dr. J. Bolling Jones, of Petersburg. The new medical quarters at the University are to be dedicated on the first day of our meting, which fact wil add greatly to the interest of those who attend, as many notable speakers will be on hand for this occasion.

Plans are also being made to have some interesting clinics and an excellent program altogether is expected. It is not too early to begin making plans to attend this meeting. Come early and stay through the three days so as not to miss anything.

Dr. and Mrs. W. J. Wiginton,

Java, Va., have returned from a two weeks' vacation spent at Miami, Fla.

Dr. John R. Gill,

Of the class of '27, University of Virginia, Department of Medicine, is now connected with the medical staff of the East Louisiana State Hospital at Jackson, La.

South Boston Hospital.

The new addition to the South Boston Hospital, owned and operated by Dr. R. H. Fuller, was formally opened March 8, 1929. This hospital was originally opened in May, 1927, as an eighteen bed hospital. The new addition brings the hospital capacity up to forty beds. The new structure is fire-proof throughout and is supplied with the newest type of equipment. The staff has been augmented to take care of the requirements entailed by the institution's growth. Dr. W. R. Counts is Resident Physician and Miss Rose Fuller, R. N. is Superintendent.

Dr. Ward C. Curtis,

Of the class of '20, Medical College of Virginia, after sometime spent at San Angelo, Texas, has moved to El Paso, Texas, where he is associated in practice with Drs. Will P. Rogers, G. H. and Sherod Mengel, with offices at 314 Roberts Banner Building.

The Southwestern Virginia Medical Society

Is to hold its Spring meeting in Pulaski, March the 27th and 28th, under the presidency of Dr. A. M. Showalter, of Christiansburg. Invited guests for this meeting are Drs. W. H. Park, of New York City, and Dr. J. S. Horsley, Sr., Richmond. Members who will take part in the symposium are: Drs. R. A. Morison, Abingdon; K. D. Graves, Pearisburg; J. W. Preston, Roanoke; and D. S. Divers, Pulaski. Those on the program for voluntary papers are: Drs. T. J. Hughes, Frank Helvestine, L. D. Keyser, R. H. DuBose and A. P. Jones, of Roanoke; Dr. D. B. Stuart, Dublin; Dr. A. B. Grubb, Cripple Creek; and Dr. H. W. Bachman, Bistol.

Dr. Drewery Ill.

As we go to press, we learn that there has been a slight change for the better in the condition of Dr. William F. Drewry, of Petersburg, Va., who has been critically ill with double pneumonia with heart complications.

Dr. Thomas E. Hughes,

Richmond, Va., sailed early this month for England to attend the running of the grand national steeplechase at Aintree.

Registered for Post-Graduate Course:

Following is a list of doctors who have registered to attend the course of post-graduate instruction to be held by Gill Memorial Hospital of Roanoke, Va., April 8th-13th, inclusive:

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Dr. C. G. Butler, Gainesville, Ga.
Dr. S. Kirkpatrick, Selma, Ala.
Dr. V. C. Dail, Knoxville, Tenn.
Dr. A. M. Walker, Tuskaloosa, Ala.
Dr. Martin Crook, Spartanburg, S. C.
Dr. Thos. W. Davis, Winston-SaSlem, N. C.
Dr. W. W. Perdue, Mobile, Ala.
Dr. E. L. Sutherland, Lynchburg, Va.
Dr. E. Vermillion, Welch, W. Va.
Dr. Wallace Gill, Richmond, Va.
Dr. L. W. Hovis, Charlotte, N. C.
Dr. Karl S. Blackwell, Richmond, Va.
Dr. Carl Bishop, Plainfield, N. J.
Dr. R. W. Petrie, Lenoir, N. C.
Dr. J. R. Perkins, Winston-Salem, N. C.
Dr. J. R. Vermillion, Princeton, W. Va.
Dr. V. F. Crouch, Winston-Salem, N. C.
Dr. J. Sidney Hood, Gastonia, N. C.
Dr. E. G. Campbell, Johnson City, Tenn.
Dr. Ogg, Johnson City, Tenn.
Dr. Darrell Harvey, Providence, R. I.
Dr. J. H. Fitzgerald, Smithfield, N. C.

Summer Institute for Colored Midwives in South Carolina.

It is hoped that a permanent midwives' school will be the outcome of the institutes for colored midwives held during the summers of 1927 and 1928 at the Vorhees School for Negroes in Denmark, S. C. The institute for 1927 was held only during July, but the 1928 institute held sessions during June, July, and August, teaching three groups of thirty midwives each. It was conducted by the maternity and infancy nurses, with a local physician and a graduate colored nurse in charge. Since 1925 the maternity and infancy nurses have conducted a prenatal clinic for mothers at the hospital connected with the Vorhees School.

Dr. Margaret P. Kuyk,

Richmond, Va., was recently elected a member of the Epsilon Chapter of the Phi Beta Kappa at the University of Richmond, in which school she is Professor Emeritus in Physiology and Hygiene.

Portland Session, A. M. A.

Plans are progressing splendidly for the Portland, Ore., meeting of the American Medical Association, dates of which are July 8th to 12th, inclusive. The Portland committee of arrangements is anxious that visitors make plans to stay over after adjournment of the sessions that they may take in some of the side trips to be enjoyed in that section. Many hotel reservations have already been made and fellows who expect to attend are urged to make reservations soon as possible that they may get accommodations in hotels of their choice. The summer excursion fares from the East will be in force at time of this meeting, and many doctors and their families are expected to take advantage of this fact to attend the Portland meeting.

Those desiring to have scientific exhibits at this meeting should send applications for same to the Director of Scientific Exhibits of the American Medical Association, 535 N. Dearborn Street, Chicago, before April the 1st, in order that the amount of space available may be apportioned to the best advantage to all concerned.

Dr. Allan M. Kimbrough,

Formerly of Richmond, Va., has located in Norfolk, Va., with offices at 201 West Freemason Street, where he will limit his work to orthopedics. Dr. Kimbrough has just returned from New York where he spent two years in post-graduate study at the New York Orthopedic Dispensary and Hospital under Dr. Russell A. Hibbs.

Dr. Mark W. Peyser,

Richmond, Va., recently visited Washington, D. C., and inspected the physiotherapy departments of various hospitals with a view to the establishment of such a department at Stuart Circle Hospital, this city.

Dr. R. E. Booker,

Of Lottsburg, Va., after a visit in Florida, returned to a Richmond hospital for treatment.

Dr. J. M. Emmett,

Clifton Forge, Va., has been named by the mayor of that place as a member of the Committee in charge of the welfare work of that city for the coming year.

Victoria, Australia, Battles Against Maternal Mortality.

During the five years ending with 1927 the Victorian Bush Nursing Association of the State of Victoria, Australia, attended 2,273 confinements of white mothers without the loss of a single mother. This organization was started in 1910 for work in the rural districts of the State, and its efforts have been so successful that in 1927 the sparsely settled "bush" had the lowest maternal mortality rate in Victoria, while the city of Melbourne, which contains more than half the population of the State, had the highest. The average rate for the State was 5.58 per 1,000 live births, which contrasts favorably with the rate during the same year, 6.47, for the birth-registration area of the United States.

The successful record is attributed to the adequate training of both doctors and nurses and their excellent co-operation, insistence on continuous antenatal supervision, and properly planned, staffed, and equipped hospitals to which all complicated cases are removed at the earliest moment.

The American Association for the Study of Goiter

Is to hold its annual meeting in Dayton, Ohio, March 25th, 26th and 27th, with headquarters at the Miami Hotel. Dr. S. D. Van Meter, Denver, Col., is president, and Dr. F. B. Dorsey, Jr., Keokuk, Iowa, recording secretary. In addition to a number of interesting papers, operative clinics will be held on the morning of the 26th.

Married.

Dr. Harry Hudnall Ware, Jr., and Miss Mary Warren Williams, both of Richmond, Va., February the 16th.

Graduate Fortnight of the New York Academy of Medicine.

The New York Academy of Medicine is arranging for a second series of lectures at the Academy, co-ordinated clinics, clinical demonstrations and courses in hospitals and teaching institutions of New York, on the subject of "Functional and Nervous Problems in Medicine and Surgery". The fortnight will be held during the period October 7 to 19, 1929.

Evening sessions will be held at the Academy at which well known authorities will discuss many phases of the general subject. During the mornings and afternoons specially prepared clinical programs will be presented in a number of the leading hospitals of the city.

The profession is generally invited to attend. No fee will be charged for attendance at any of the meetings or clinics on the program.

Medical College of Virginia News.

President Edwin A. Alderman, University of Virginia, will deliver the principal address at the ninety-first commencement of the Medical College of Virginia, Richmond, on Tuesday, May 28, 1929.

The Chemical Foundation, Inc., of New York City, has made a grant to the Medical College of Virginia, Richmond, to make it possible to employ for a three year period, a full time expert to enlarge its present program of research in chemistry as related to medicine, surgery, and dentistry. The special laboratory for this work will also be considerably enlarged.

How Many School Children Have Heart Disease?

The prevalence of heart disease among the school children of this country has had little investigation. A recent examination of approximately 120,000 Boston children of school age showed that 785 had organic heart disease. Routine examination of school children in New York City indicates that seven in every 1,000 have diseased hearts—the same rate as was discovered in 1924 among children in the elementary schools of England and Wales. The Heart Committee of the New York Tuberculosis and Health Association, which recently published these figures, calls attention to the importance for such children of education beyond the elementary grades, so that they may be able to find work and amusement which will not unduly strain the heart.

Texas Studies Its Mexican Children.

A grant from the Laura Spelman Rockefeller Memorial Fund has enabled the School of Education of the University of Texas to undertake a study of the education of children of Mexican immigrants in Texas.

Dr. Phil H. Neal,

Of the Medical College of Virginia, class of '23, after several years of post-graduate work in New York City, has become associated with Dr. Stuart L. Craig, 135 East Sixty-Fifth Street, that city. His practice is limited to diseases of the ear, nose and throat.

Dr. M. B. Hiden,

Warrenton, Va., has been appointed by the local Chamber of Commerce as a member of a committee to prepare a pamphlet or book which will set forth the advantages of Warrenton and vicinity.

The American College of Physicians

Will hold its thirteenth annual clinical session in Boston, April 8th-12th, under the presidency of Dr. Charles F. Martin, Dean of the Faculty of Medicine, McGill University. Dr. John H. Musser, Professor of Medicine at Tulane University Medical School, is president-elect and will be inducted to the presidency toward the end of the Boston meeting. Dr. James H. Means, Jackson Professor of Clinical Medicine at Harvard Medical School and Chief of the Medical Service at the Massa-

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chusetts General Hospital, is General Chairman of all Boston Committees.

Dr. J. Morrison Hutcheson, Richmond, is the Virginia member of the Board of Governors of the College.

The Program provides hospital visits, clinics, demonstrations and ward-walks during the forenoons at fifteen different Boston hospitals, and for general scientific sessions each afternoon and evening in the Assembly Room of the Hotel Statler, which will he headquarters.

A Symposium on Deficiencies will take place the first evening of the session. Another special feature is a review of the Present Status of Vaccine and Serum Prophylaxis and Therapy by Dr. Benjamin White, of Boston, an authority on these subjects. The annual banquet of the College will be held Thursday evening, April 11th, when Dr. George E. Vincent, President of the Rockefeller Foundation, will deliver the chief address. The Convocation, for the conferring of Fellowships, will take place Friday evening, April 12th.

Programs and details concerning reduced fares, admission, etc., may be secured from the Executive Secretary, E. R. Loveland, 133-135 S. 36th Street, Philadelphia, Pa.

Free Book for Medical Students Who Intend to Visit Hungary.

A guide book for physicians and medical students who intend to visit Hungary is being distributed gratis by the Cunard Line. It gives full information concerning the conditions under which members of the medical profession may continue their studies in Budapest, giving courses which may be taken up at the various clinics and universities. The book may be obtained by dropping a card to the Cunard Line, 25 Broadway, New York.

Dr. Edward W. Rawls,

Portsmouth, Va., has been elected a member of the Second District congressional committee.

Cardiac Conferences.

Believing in the teaching function of hospitals not located in medical teaching centers, a series of three weekly cardiac conferences were recently held at the Montgomery Clinic, Montgomery, W. Va., under the direction of Dr. Milton C. Borman.

The conferences were well attended by physicians from various parts of the county. The diagnosis and treatment of diseases of the heart muscle and cardiac valvular disease, and the recognition, importance, and treatment of the various cardiac arrhythmias were presented. Ambulatory and hospital patients were shown, and gross pathological specimens and microscopic slides of cardiac lesions were demonstrated with a projectoscope.

Dr. Andrew F. Giesen,

Recently of Brownsburg, Va., has moved to Konawa, Okla., where he is associated in general practice with Dr. W. J. Long.

Base Hospital No. 45, of the Veterans' Association,

Familiarly known as the McGuire Unit, held its annual reunion in Richmond on March the 2nd. Memorial services for all deceased members were held at the grave of Dr. E. Guy Hopkins in Hollywood Cemetery. Dr. and Mrs. Stuart McGuire entertained the members at a reception at their home in the afternoon. This was followed by a banquet at the Commonwealth Club at which time Dr. Robert C. Bryan, Richmond, was the principal speaker.

Results From Christmas Seal Sales.

It was announced at the office of the Virginia Tuberculosis Association at Richmond that the sale of tuberculosis Christmas Seals for 1928 was the largest ever held in Virginia.

The Executive Secretary, Miss Leslie C. Foster, stated that a great many of the county and city chairmen reported their sales were seriously curtailed by the epidemic of influenza which was at its height during the period when seals were being sold. Many of the volunteer workers were ill and the schools, which assist in the country districts, were closed. In spite of this handicap, the amount received to date is $64,888.70, with small amounts still coming in, and it is expected the sale will certainly reach $65,000—an increase of nearly $2,000 over the 1927 sale.

Dr. A. M. Byrd

Recently returned to his home at Northfork, W. Va., after attending a genito-urinary clinic of the U. S. Public Health Service at Hot Springs, Ark., to which place he had an appointment by the State of West Virginia. After completing his work there, Dr. Byrd visited many places of interest in the Southwestern part of the United States.

International Congress of Mental Hygiene.

Plans are already being made for the first International Congress on Mental Hygiene, to

be held in Washington, D. C., in May, 1930. It is stated that national organizations for mental hygiene have been or are being established in twenty-one countries besides the United States and Canada and that all important countries will undoubtedly be represented by such agencies at this congress. Information about the meeting may be obtained from Mr. Clifford W. Beers, secretary of the National Committee for Mental Hygiene, 370 Seventh Avenue, New York City.

Dr. Francis W. Upshur,

Richmond, Va., recently resigned as executive surgeon of the Virginia Electric and Power Company after having been connected with the surgical staff of this company for twenty-six years. Dr. Upshur is now devoting his whole time to private practice.

The American Proctologic Society

Will hold its annual meeting in Detroit, Mich, May 13th, 14th and 15th, under the presidency of Dr. Edward G. Martin, of that city. All reputable medical men will be welcomed as guests at this meeting. Dr. Walter A. Fansler, Minneapolis, Minn., is secretary.

Improved Trachoma Conditions in Kentucky.

According to a report published by the National Society for the Prevention of Blindness, increased medical facilities and widespread education on matters of hygiene throughout Kentucky have reduced the number of trachoma sufferers in that state from an estimated 50,000 persons to less than 3,000 in the last fifteen years. It is stated that the mountaineers have been taught the symptoms of trachoma and have learned thus to secure treatment for this disease in its early stages, at which time it may be cured. This great reduction in the number of cases of trachoma has apparently been instrumental in bringing about a higher standard of living.

Dr. A. L. Tynes

Has returned to his home in Staunton, Va., after several weeks spent at Coral Gables, Fla., where he went to recuperate from the effects of a severe case of influenza.

Dr. Guy R. Harrison,

Of Richmond, dental member of the Virginia State Board of Health and oral surgeon to St. Luke's and Stuart Circle Hospitals, this city, by invitation addressed the Virginia Tidewater Dental Association in Norfolk, at its meeting on February the 21st.

Dr. A. M. Showalter,

Christiansburg, Va., is one of the line grand officers of the Grand Lodge of Virginia, A. F. and A. Masons, and according to custom, was elevated one rank, at the meeting of the Grand Lodge in Richmond, the middle of February.

The American Climatological and Clinical Association

Is to hold its annual meeting at the Chamberlin-Vanderbilt Hotel, Old Point Comfort, Va., May 2, 3 and 4, 1929, under the presidency of Dr. J. Woods Price, of Saranac Lake, N. Y. Dr. Arthur K. Stone, Framingham Center, Mass., is secretary of the Association.

Dr. H. R. Farley,

Pulaski, Va., left the last of February for New York City, for the purpose of taking up post-graduate work.

Dr. and Mrs. Julian M. Robinson

Recently returned to their home in Danville, Va., after a visit to Cuba.

Dr. C. T. Carter,

Of Danville, Va., who has been visiting in Havana, is now in Florida in which place Mrs. Carter has joined him.

Dr. C. B. Bowyer,

Who has been spending part of his winter vacation in Havana, Cuba, will return to his home at Stonega, Va., shortly.

Dr. F. Thomas Amiss,

Recently of St. Charles, Va., has moved to Luray, Va., where he will continue the practice of his profession.

The Mid-Tidewater Medical Society,

Composed of the counties in the peninsula between the York and Rappahannock Rivers and also York and New Kent Counties, will hold its regular quarterly meeting at Mathews C. H., Wednesday, April the 24th. Dr. Hawes Campbell, Enfield, is president, and Dr. Malcolm H. Harris, West Point, secretary.

Civil Service Examinations.

The U. S. Civil Service Commission, Washington, D. C., announces an open competitive examination for associate medical officer and assistant medical officer, applications for same to be on file with the Commission not later than June 29th. Competitors will not be required to report for examination, but will be rated on their education, training and experience. Full information may be secured of the above named Service.

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Boys' Club to Fight Juvenile Delinquency in Chicago.

The erection of twenty-five new boys' club buildings in the congested districts of Chicago is planned by the Chicago Boys' Club, in a campaign to reduce juvenile delinquency in that city. Each club building is to cost $200,000 and will contain a gymnasium, swimming pool, game rooms, playgrounds, and other equipment. It is expected that the buildings will be completed during the next five years.

Playgrounds for the Holy Land.

In 1926 a playground furnished with American equipment and under the charge of a trained director was established under the wall of the Old City of Jerusalem just within Zion Gate. Here 600 boys and girls of many races, religions, and classes are learning to play together. Mrs. Bertha Guggenheimer, who died soon after the opening of the playground, left $100,000 to be used for its maintenance and that of others to be established. A playground is planned for the new part of Jerusalem outside the walls and one for Tel Aviv, a wholly new Jewish city founded in 1910.

Dr. Toson O. Summers,

Formerly of Richmond, Va., now lieutenant commander in the U. S. Navy, sailed early this month from Norfolk, Va., for St. Thomas, the Virgin Islands, where he will be stationed for the next two years.

Wanted to Buy—

Physician's combined residence and office property in city of between five and ten thousand population. Address No. 158, care this journal. (*Adv.*)

Obituary Record

Dr. Homer Silon Henkel,

Staunton, Va., died in Baltimore, Md., February the 12th, after a lingering illness with heart disease. Dr. Henkel was born in Staunton, forty-three years ago and, after attending school at the Staunton Military Academy, studied medicine at the Medical College of Virginia, from which he graduated in 1914. He practiced for six years at Brownsburg after which he took a post-graduate course in New York. On hs return, he located in Staunton and he and Dr. G. R. Fisher formed a partnership and limited their work to diseases of the eye, ear, nose and throat. He was a member of the Medical Society of Virginia. His wife and a daughter survive him.

Dr. Lyndsay Wolford Newland,

Of Splashdam, Va., member of the Medical Society of Virginia, died December the 24th, after a short illness with pneumona. He was forty-one years of age and was graduated in medicine from Lincoln (Nebr.) Medical College in 1911. Dr. Newland served throughout the World War. At the time of his death he was secretary-treasurer of the Dickenson-Buchanan County Medical Society.

Dr. John J. Nelson, Sr.,

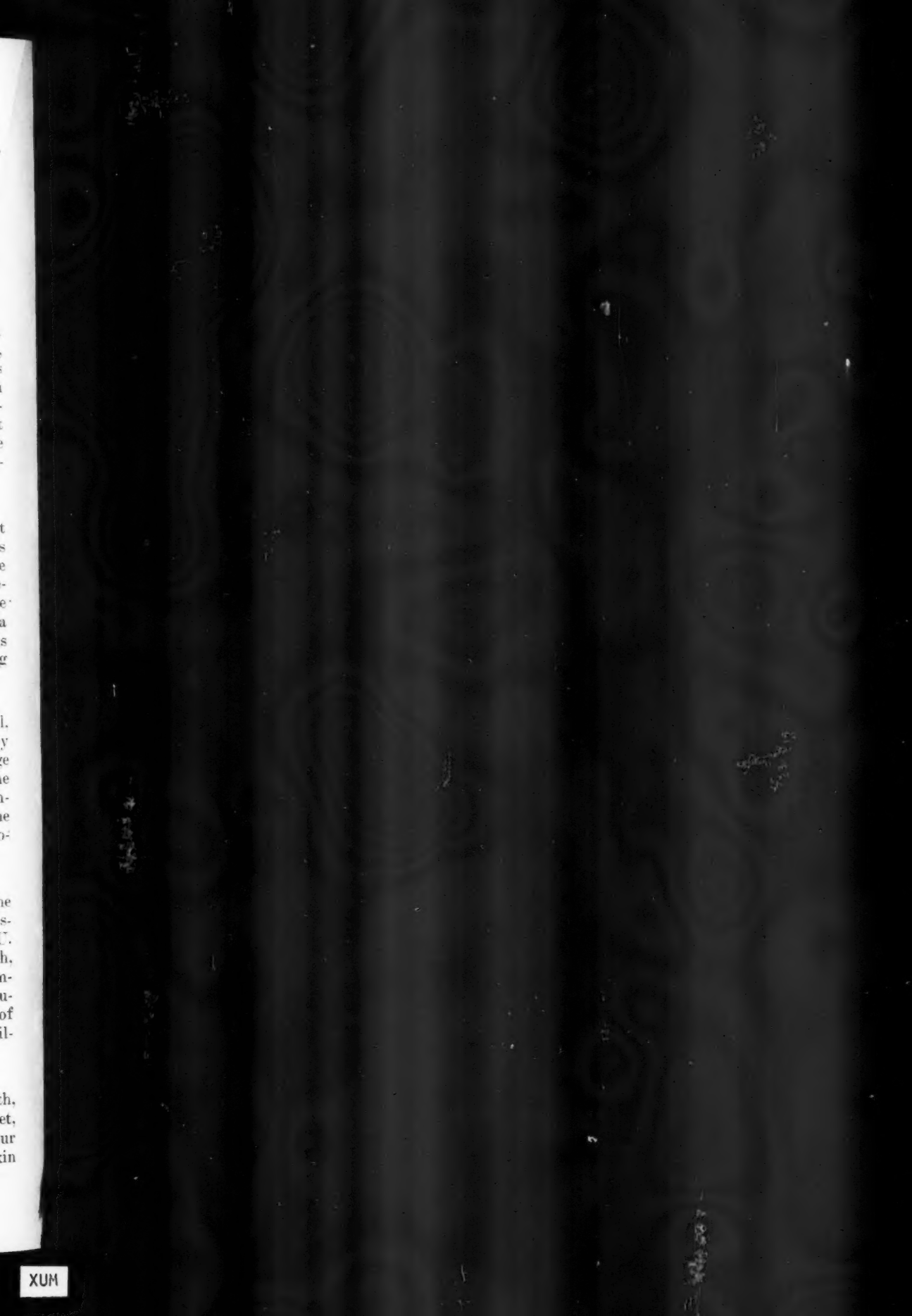
Columbia, Va., died at his home in that place on February the 15th, after an illness of several years. He studied medicine at the University of Virginia, from which he received his diploma in medicine in 1876. He had practiced in the section around Columbia for forty-five years. He is survived by his wife and several children, one of them being Dr. J. J. Nelson, Jr., also of Columbia.

Dr. Paul Clenton Brittle,

Burlington, N. C., died at a local hospital, January the 29th, following an emergency operation. He was forty-nine years of age and had graduated in medicine from the former University College of Medicine, Richmond, Va., in 1907. He was a member of the Medical Society of the State of North Carolina.

Dr. William Thomas Williamson,

For the past eight years in charge of the department of medicine and cardovascular diseases of the Richmond (Va.) office of the U. S. Veterans' Bureau, died February the 17th, death being due to pneumonia. Dr. Williamson was sixty-four years of age and a graduate of the University of Louisville, School of Medicine, in 1886. His wife and several children survive him.

Professor Clemens von Pirquet.

Announcement has been made of the death, early this month, of Professor von Pirquet, renowned Austrian pediatrist, aged fifty-four years. He was the inventor of the serum skin test for tuberculosis.